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QUALITY CONTROL OF PET CAMERA FOR SMALL ANIMAL IMAGING

EFTHIMIOU NIKOLAOS

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ABSTRACT

The term Molecular Imaging (MI) can be broadly defined as the in vivo characterization and measurement of biological processes at the cellular and molecular level. In contradistinction to “classical” diagnostic imaging, it sets forth to probe the molecular abnormalities that are the basis of disease rather than to image the end effects of these molecular alterations. The underlying biology represents a new arena for many researchers. A number of technological challenges such as signal amplification, data and image processing and efficient imaging strategies, provide a fast growing scientific domain. Positron Emission Tomography (PET), Magnetic Resonance Imaging (MRI), Single Photon Emission Tomography (SPECT) and optical imaging are the main tools of clinical molecular imaging. Nuclear medicine techniques (SPECT and PET) are key players in MI. New radiopharmaceutical products are currently being developed, in order to increase the specificity and sensitivity of existing imaging techniques. Small animal imaging is the main tool for the evaluation of those derivatives, especially in dynamic in vivo studies. In this, preclinical part, high resolution and high sensitivity imaging equipment is necessary; as a result a number of such prototypes have been developed worldwide and some of them are commercialized. However, there cost is usually not affordable for small or medium size laboratories.

In this work a low cost dual head PET camera, suitable for high resolution small animal studies has been developed. It is the result of the collaboration between Jefferson lab and Technological Educational Institute of Athens (TEI) and is currently evaluated in Institute of Radioisotopes and Radiodiagnostic Products (IRRP), in “Demokritos” Center.

The system has a field of view of 5x5cm and is based on 2 H8500 position sensitive photomultiplier tubes (PSPMTs), coupled to two LSO crystals with 2.5x2.5mm pixel size. Then an FPGA based data acquisition system and proper data reconstruction system collect events, sort coincidences and produce images. The DAQ board consists of 16-channel DAQ modules installed on a USB2 carrier. Each channel is an independent acquisition system consisting of traditional analog pulse processing, FPGA analog control, and FPGA signal processing. After acquisition and processing, channel data are assembled into event blocks for readout by the carrier board. Application specific tasks are performed in JAVA using the Kmax interface. The GUI was designed to be easy-to-use. In order to further analyze images and process the results proper algorithms were developed in MATLAB and ImageJ. Systems evaluation has been carried out using FDG. Point sources have been used for systems calibration. Capillaries with 1.1mm inner diameter were imaged and used for resolution calculation. Finally a mouse injected with 100μCi of FDG was imaged. Spatial resolution has been measured using thin capillaries (1.1mm inner diameter) and found equal to 3.5mm in planar mode. This lower limit is determined by LSO pixels size (2.5×25mm²). Simulation studies have shown that resolution lower than 2mm will be achieved in tomographic mode. Mice injected with FDG are presented. Brain and heart are clearly imaged.

Currently, a rotating base is constructed, in order to upgrade the system to a tomographic PET. PET results will be presented as well. In addition, IRRP and TEI are working on new radiopharmaceuticals based on Cu-64. It must be stated that PET market opened in Greece four years ago; This system is the first working small PET prototype in Greece and it initiates national preclinical PET research.
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1 Introduction

1.1 Small animal Imaging Review

More than a decade ago, several research groups started to develop Positron Emission Tomography (PET) systems dedicated to small animal imaging. The growing interest in pre-clinical imaging studies, both in biological and medical basic research, in pharmaceutical industry, as well as in radiophysics and biomedical engineering community has recently induced the world-leading manufacturers of medical image equipment to invest in this market. Some of the proposed scanner prototypes in an overhauled and/or enhanced version, turned into commercial systems, and five PET scanners dedicated to small animals (mice and rats) are today commercially available: “Explore Vista” from General Electric Healthcare (Waukesha, Wisconsin, USA), “microPET Focus” from Concorde Microsystems, Inc., (Knoxville, Tennessee, USA), “quad-HIDAC” from Oxford Positron Systems Ltd. (Weston-on-the-Green, Oxfordshire, UK), “Mosaic” from Philips Medical Systems (Milpitas, California, USA) and “Yap- PET” from I.S.E. Srl (Migliarino Pisano, Pisa, Italy).

Small animal positron emission tomography (PET) scanners have been developed to perform imaging of anatomical structures that are smaller than those in humans. The linear dimensions of an organ such as the brain in mice, rats, rabbits and lately even monkeys are respectively, nearly 8 times and 14 times smaller than in human subjects. It follows that a clinical PET scanner is not suitable to conduct studies on small animals. On the other hand, the availability of a dedicated machine for animals has the advantage to allow the use of the tomograph for laboratory experiments at all times and to work in a physically different environment from that used for humans as required by the regulatory authorities. A dedicated small animal PET is only seemingly considered as a miniaturized clinical PET. The need to achieve a much higher resolution both spatial and energy and at the same time a good sensitivity represents a trivial task. In terms of the design, the reduced size of the gantry offers some advantages. It is known that the maximum spatial resolution is limited in PET by the acolinearity of the two annihilation photons, besides the positron range. Reducing the distance between the detectors, (e.g. reducing the ring diameter in ring-type scanners) the effect of the 511 keV photons acolinearity on the system resolution can be reduced, this also affects the parallax effect which also is degraded. The other advantage is a raw material saving due to the smaller size of the system.

The detection systems of PET have mostly been developed using scintillator materials. Inorganic crystals such as BGO, LSO(Ce) and GSO(Ce) have been employed in the construction of human scanners and then used for small animal PET scanners. Other scintillator materials have been investigated such as LGSO(Ce), a material with properties similar to LSO and the YAP(Ce), a scintillator with some favorable properties but a relatively low detection efficiency for 511 keV photons, used for small animal PET scanner prototype and chosen for the production of a hybrid system PET/single photon emission computed tomography (SPECT) dedicated to rodents.

At the same time, a reduction in the scintillator size increases the fraction of gamma rays obliquely incident on the detector surface, causing the parallax error that degrades the spatial resolution from the center towards the edge of the field of view. Non-uniformity in the spatial resolution can be restored by measuring the depth-of-interaction of the photons. To do this, phosphor sandwich (phoswich) detectors have been developed. A dual layer phoswich detector is composed of two joined scintillators with different decay time constants. By discriminating on the pulse shape, one can distinguish the depth-of-interaction of gamma rays. For instance, a dual layer phoswich of LSO crystals of different decay time has been used for a commercial human “brain dedicated” PET tomograph by Siemens; a phoswich with two layers of different scintillators LGSO and GSO has been used for a commercial small animal PET. Considerable effort has been put into the coupling scheme scintillator photomultiplier tube, in order to optimize light collection or to simplify the design and maintenance of
a PET detection system. The block detector represents a breakthrough that gave a modular structure to a detector ring reducing the number of photomultiplier tubes required.

In regard to the possibility to use gamma rays detectors as alternative to scintillators coupled to photomultipliers, one group has proposed a modified version of a position sensitive gas ionization chamber. In this kind of detector, known as the high density avalanche chamber (HIDAC), the incident gamma rays are “converted” by cathode plates into electrons and then detected and localized collecting the ionization generated by these in the gas. Cathode plates are formed by layers of laminated lead containing interleaved insulated sheets, mechanically drilled with typically 200 000 holes (0.4 mm in diameter, 0.5 mm pitch); every hole acts as an independent detector element (equivalent to a scintillator element and a photomultiplier). The intrinsic spatial resolution of an HIDAC detector primarily depends on the hole pitch. In order to achieve a high spatial resolution in a scintillator based small animal PET scanner, the size of the scintillator crystals cross section must be reduced compared to a human tomograph. As a consequence, the solid angle covered by a single small area detector element is lower, thus decreasing the sensitivity.

More recently, the use of optical fiber coupling has been proposed to extend flexibility in the realization of scintillator array with high packing fraction. Continuous light-guide backed to an array of photomultiplier is another effective coupling scheme to improve light collection for large area continuous pixelated detectors. The possibility to use avalanche photodiodes (the solid state version of a photomultiplier tube) for the readout of scintillation crystals has also been investigated, although these are not yet implemented in commercial PET equipment. Researchers are now exploring innovative solutions regarding both hardware (detector material, detector configuration and detector read-out) and software (3D reconstruction algorithms), to build systems with improved performance characteristics.

The purpose of the current thesis was the evaluation of the a small animal PET prototype. This prototype is the first preclinical PET system here in Greece. It is not a commercially available system but is custom made and fully accessible in all of it parts.

It was developed by the

- Detector and Imaging Group, Thomas Jefferson National Accelerator Facility., USA
- Department of Medical Physics, Medical School, University of Patras
- Department of Medical Instruments Technology, Technological Educational Institution of Athens.
- Institute of Radioisotopes – Radiodiagnostic Products, N.C. S. R. “Demokritos”.

This system is planned to be used for radiopharmaceutical research as well as a base for development of novel PET scanners which will incorporate leading edge technologies.
2 Atomic Physics

2.1 The atoms

All matter is composed of atoms. Atoms themselves are complicated entities. An atom is the smallest unit of matter that retains the chemical properties of a material. The basic structure of an atom is a positively charged nucleus, containing electrically positively charged protons and neutral neutrons, surrounded by one or more negatively charged electrons. The number and distribution of electrons in the atom determines the chemical properties of the atom. The number and configuration of neutrons and protons in the nucleus determines the stability of the atom and its electron configuration.

2.1.1 Structure of the Atom

One unit of charge is $1.6 \times 10^{-19}$ coulombs. Each proton and each electron carries one unit of charge, positive and negative, respectively. The number of protons in the nucleus is termed the atomic number $Z$. The atomic number uniquely determines the classification of an atom as one of the elements.

Atoms in their normal state are neutral because the number of electrons outside the nucleus equals the number of protons of the nucleus. Electrons are positioned in energy levels (i.e. shells) that surround the nucleus. The first ($n = 1$) or K shell contains no more than 2 e, the second ($n = 2$) or L shell contains no more than 8 e, and the third ($n = 3$) or M shell contains no more than 18 e. The outermost electron shell of an atom, no matter which shell it is, never contains more than 8 e. Electrons in the outermost shell are termed valence electrons and determine to a large degree the chemical properties of the atom.

Energy levels for electrons are divided into sub levels slightly separated from each other. To describe the position of an electron in the extra-nuclear structure of an atom, the electron is assigned four quantum numbers.

The principal quantum number $n$ defines the main energy level or shell within which the electron resides ($n = 1$ for the K shell, $n = 2$ for the L shell, etc.). The orbital angular-momentum (azimuthal) quantum number $l$ describes the electron’s angular momentum ($l = 0, 1, 2, \ldots, n-1$). The orientation of the electron’s magnetic moment in a magnetic field is defined by the magnetic quantum number $m_l$ ($m_l = -l, -l+1, \ldots, l-1, l$). The direction of the electron’s spin upon its own axis is specified by the spin quantum number $m_s$ ($m_s = +1/2$ or $-1/2$). The Pauli Exclusion Principle states that no two electrons in the same atomic system may be assigned identical values for all four quantum numbers.

The values of the orbital angular-momentum quantum number, $l = 0, 1, 2, 3, 4, 5$ and $6$, are also identified with the symbols, $s, p, d, f, g,$ and $i,$ respectively. This notation is known as “spectroscopic” notation because it is used to describe the separate emission lines observed when light emitted from a heated metallic vapor lamp is passed through a prism. In the presence of a magnetic field, the $p$ “orbital” can be in alignment along any one of three axis of space, $x,$ $y,$ and $z.$ Each of these three orientations has a slightly different energy corresponding to the three possible values of $m_l$ ($-1, 0,$ and $1$). According to the Pauli exclusion principle, each orbital may contain two electrons (one with $m_s = +1/2$, the other with $m_s = -1/2$).
2.2 The Nucleus

2.2.1 Nuclear Energy Levels

A nucleus consists of two types of particles, referred to collectively as nucleons. The positive charge and roughly half the mass of the nucleus are contributed by protons. Each proton possesses a positive charge of $+1.6 \times 10^{-19}$ coulombs, equal in magnitude but opposite in sign to the charge of an electron. The number of protons positive charges in the nucleus is the atomic number of the atom.

The mass of a proton is $1.6734 \times 10^{-27}$ kg. Neutrons, the second type of nucleon, are uncharged particles with a mass of $1.6747 \times 10^{-27}$ kg. Outside the nucleus, neutrons are unstable and divide into protons, electrons, and anti-neutrinos. The half-life of this transition is 12.8 minutes. Neutrons are usually stable inside nuclei. The number of neutrons in a nucleus is the neutron number $N$ for the nucleus. The mass number $A$ of the nucleus is the number of nucleons in the nucleus.

\[ A = Z + N \quad (2.2.1-1) \]

Expressing the mass of atomic particles in kilograms is unwieldy because it would be a very small number requiring scientific notation. The atomic mass unit (amu) is a more convenient unit for the mass of atomic particles. 1 amu is defined as 1/12 the mass of the carbon atom, which has six protons, six neutrons, and six electrons.

\[ 1 \text{ amu} = 1.6605 \times 10^{-27} \text{ kg} \quad (2.2.1-2) \]

The shell model of the nucleus was introduced to explain the existence of discrete nuclear energy states. In this model, nucleons are arranged in shells similar to those available to electrons in the extranuclear structure of an atom. Nuclei are extra-ordinarily stable if they contain 2, 8, 14, 20, 28, 50, 82, or 126 protons or similar numbers of neutrons. These numbers are termed magic numbers and may reflect full occupancy of nuclear shells. Nuclei with odd numbers of neutrons or protons tend to be less stable than nuclei with even numbers of neutrons and protons. The pairing of similar nucleons increases the stability of the nucleus.

2.2.2 Nuclear Forces and Stability

Protons have the same type of charge, so repel each other by the electrostatic force of repulsion. The nucleus doesn't split because of the fact that when protons are very close together, a powerful attractive force comes into play. This force, called the “strong nuclear force,” is 100 times greater than the electrostatic force of repulsion. However, it acts only over distances of the order of magnitude of the diameter of the nucleus. Therefore, protons can stay together in the nucleus once they are there. Assembling a nucleus by forcing protons together requires the expenditure of energy to overcome the electrostatic repulsion. Neutrons, having no electrostatic charge, do not experience the electrostatic force. Therefore, adding neutrons to a nucleus requires much less energy.

2.2.3 Nuclear Binding Energy

The mass of an atom is less than the sum of the masses of its neutrons, protons, and electrons. This seeming paradox exists because the binding energy of the nucleus is so significant compared with the masses of the constituent particles of an atom, as expressed through the equivalence of mass and energy described by Einstein’s famous equation.

\[ E = mc^2 \quad (2.2.3-1) \]
The mass difference between the sum of the masses of the atomic constituents and the mass of the assembled atom is termed the mass defect. When the nucleons are separate, they have their own individual masses. When they are combined in a nucleus, some of their mass is converted into energy. In Einstein’s equation, an energy \( E \) is equivalent to mass \( m \) multiplied by the speed of light in a vacuum, \( c (2.998\times10^8 \text{ m/sec}) \) squared. Because of the large “proportionality constant” \( c^2 \) in this equation, one kilogram of mass is equal to a large amount of energy, \( 9\times10^{16} \text{ joules} \). The energy equivalent of 1 amu is

\[
\frac{(1 \text{ amu})(1.660\times10^{-27} \text{ kg/amu})(2.998\times10^8 \text{ m/sec})}{(1.602\times10^{-13} \text{ J/MeV})} = 931 \text{ MeV} \tag{2.3-2}
\]

### 2.3 Nuclear Fission and Fusion

Energy is released when a nucleus with a high mass number separates, or fissions, into two parts, each with an average binding energy per nucleon greater than that of the original nucleus. The energy release occurs because such a split produces low-Z products with a higher average binding energy per nucleon than the original high-Z nucleus. A transition from a state of lower “binding energy per nucleon” to a state of higher “binding energy per nucleon” results in the release of energy. However, the energy available from a transition between nuclear energy levels is orders of magnitude greater than the energy released during electron transitions.

Certain high-A nuclei (e.g., \( ^{235}\text{U} \)) fission spontaneously after absorbing a slowly moving neutron. For \( ^{235}\text{U} \), a typical fission reaction is:

\[
^{235}_{92}\text{U} + \text{neutron} \rightarrow ^{236}_{92}\text{U} \rightarrow ^{141}_{56}\text{Ba} + 3\text{neutrons} + Q \tag{2.3-1}
\]

The energy released is designated as \( Q \) and averages more than 200 MeV per fission. The energy is liberated primarily as \( \gamma \) radiation, kinetic energy of fission products and neutrons, and heat and light. Products such as \(^{92}_{36}\text{Kr} \) and \(^{141}_{56}\text{Ba} \) are termed fission byproducts and are radioactive. Many different byproducts are produced during fission. Neutrons released during fission may interact with other \(^{235}\text{U} \) nuclei and create the possibility of a chain reaction, provided that sufficient mass of fissionable material (a critical mass) is contained within a small volume. The rate at which a material fissions, may be regulated by controlling the number of neutrons available each instant to interact with fissionable nuclei.

Certain low-mass nuclei may be combined to produce a nucleus with an average binding energy per nucleon greater than that for either of the original nuclei. This process is termed nuclear fusion and is accompanied by the release of large amounts of energy. A typical reaction is:

\[
^3_1\text{H} + ^3_1\text{H} \rightarrow ^4_2\text{He} + \text{neutron} + Q \tag{2.3-2}
\]

In this particular reaction, \( Q = 18 \text{ MeV} \).

To form products with higher average binding energy per nucleon, nuclei must be brought sufficiently near one another that the nuclear force can initiate fusion. In the process, the strong electrostatic force of repulsion must be overcome as the two nuclei approach each other. Nuclei moving at very high velocities possess enough momentum to overcome this repulsive force. Adequate velocities may be attained by heating a sample containing low-Z nuclei to a temperature greater than \( 120 \times 10^6 \text{ K} \), roughly
equivalent to the temperature in the inner region of the sun. Temperatures this high may be attained in the center of a fission explosion. Consequently, a fusion (hydrogen) bomb is “triggered” with a fission bomb. Controlled nuclear fusion has not yet been achieved on a macroscopic scale, although much effort has been expended in the attempt.

2.4 Nuclear Nomeclature

Isotopes of a particular element are atoms that possess the same number of protons but a varying number of neutrons. For example, $^1\text{H}$ (protium), $^2\text{H}$ (deuterium), and $^3\text{H}$ (tritium) are isotopes of the element hydrogen.

Isotones are atoms that possess the same number of neutrons but a different number of protons. For example, $^5\text{He}$, $^6\text{Li}$, $^7\text{Be}$ are isotones because each isotope contains three neutrons. Isobars are atoms with the same number of nucleons but a different number of protons and a different number of neutrons. For example, $^6\text{He}$, $^6\text{Li}$ are isobars ($A = 6$). Isomers represent different energy states for nuclei with the same number of neutrons and protons.

2.5 Radioactive Decay

2.5.1 Nuclear stability and decay

The nucleus of an atom consists of neutrons and protons, referred to collectively as nucleons. In a popular model of the nucleus (the “shell model”), the neutrons and protons reside in specific levels with different binding energies. If a vacancy exists at a lower energy level, a neutron or proton in a higher level may fall to fill the vacancy. This transition releases energy and yields a more stable nucleus. The amount of energy released is related to the difference in binding energy between the higher and lower levels. The binding energy is much greater for neutrons and protons inside the nucleus than for electrons outside the nucleus. Hence, energy released during nuclear transitions is much greater than that released during electron transitions.

If a nucleus gains stability by transition of a neutron between neutron energy levels, or a proton between proton energy levels, the process is termed an isomeric transition. In an isomeric transition, the nucleus releases energy without a change in its number of protons ($Z$) or neutrons ($N$). The initial and final energy states of the nucleus are said to be isomers. A common form of isomeric transition is gamma decay, in which the energy is released as a packet of energy (a quantum or photon) termed a gamma ($\gamma$) ray. An isomeric transition that competes with gamma decay is internal conversion, in which an electron from an extra-nuclear shell carries the energy out of the atom.

It is also possible for a neutron to fall to a lower energy level reserved for protons, in which case the neutron becomes a proton. It is also possible for a proton to fall to a lower energy level reserved for neutrons, in which case the proton becomes a neutron. In these situations, referred to collectively as beta ($\beta$) decay, the $Z$ and $N$ of the nucleus change, and the nucleus transmutes from one element to another.

In all of the transitions described above, the nucleus loses energy and gains stability. Hence, they are all forms of radioactive decay. In any radioactive process the mass number of the decaying (parent) nucleus equals the sum of the mass numbers of the product (progeny) nucleus and the ejected particle. That is, mass number $A$ is conserved in radioactive decay.
2.6 Alpha Decay

Some heavy nuclei gain stability by a different form of radioactive decay, termed alpha (α) decay. In this mode of decay, an alpha particle (two protons and two neutrons tightly bound as a nucleus of Helium $^{4}\text{He}$) is ejected from the unstable nucleus. The alpha particle is a relatively massive, poorly penetrating type of radiation that can be stopped by a sheet of paper. An example of alpha decay is:

$$^{226}_{88}\text{Ra} \rightarrow ^{222}_{86}\text{Ra} + ^{4}_{2}\text{He} \quad (2.6-1)$$

This example depicts the decay of naturally occurring radium into the inert gas radon by emission of an alpha particle. A decay scheme (see below) for alpha decay is depicted in the right margin.

2.6.1 Decay Schemes

A decay scheme depicts the decay processes specific for a nuclide (nuclide is a generic term for any nuclear form). A decay scheme is essentially a depiction of nuclear mass energy on the y axis, plotted against the atomic number of the nuclide on the x axis. A decay scheme is where the generic nuclide $^{A}_{Z}X$ has four possible routes of radioactive decays:

1. α decay to the progeny nuclide $^{A+4}_{Z+2}P$ by emission of a $^{4}_{2}\text{He}$ nucleus;
2. (a) β⁺ (positron) decay to the progeny nuclide $^{A}_{Z-1}Q$ by emission of a positive electron from the nucleus;  
   (b) electron capture (ec) decay to the progeny nuclide $^{A}_{Z-1}Q$ by absorption of an extranuclear electron into the nucleus;
3. β⁻ (negatron) decay to the progeny nuclide $^{A}_{Z-1}R$ by emission of a negative electron from the nucleus.

The processes denoted as 2(a) and 2(b) are competing pathways to the same progeny nuclide. Any of the pathways can yield a nuclide that undergoes an internal shuffling of nucleons to release additional energy. This process, termed an isomeric transition, is shown as pathway 4. No change in Z (or N or A) occurs during an isomeric transition.

2.7 Beta Decay

2.7.1 Nuclear Stability

Nuclei tend to be most stable if they contain even numbers of protons and neutrons, and least stable if they contain an odd number of both. Nuclei are extraordinarily stable if they contain 2, 8, 14, 20, 28, 50, 82, or 126 protons or similar numbers of neutrons. These numbers are termed nuclear magic numbers and reflect full occupancy of nuclear shells. The number of neutrons is about equal to the number of protons in low-Z stable nuclei. As Z increases, the number of neutrons increases more rapidly than the number of protons in stable nuclei. The shell model of the nucleus accounts for this finding by suggesting that at higher Z, the energy difference is slightly less between neutron levels than between proton levels. Many nuclei exist that have too many or too few neutrons to reside on or close to the line of stability. These nuclei are unstable and undergo radioactive decay. Nuclei above the line of stability (i.e., the n/p ratio is too high for stability) tend to emit negatrons by the process of β⁻ decay. Nuclei below the line of stability (i.e., the n/p ratio is too low for stability) tend to undergo the competing processes of positron (β⁺) decay and electron capture.
2.7.2 Negatron decay

In nuclei with an \( n/p \) ratio too high for stability, a neutron, may be transformed into a proton.

\[
_{0}^{1}n \rightarrow _{1}^{1}p + _{-1}^{0}\beta + \bar{\nu} \quad (2.7.2-1)
\]

where \( _{-1}^{0}\beta \) is a negative electron ejected from a nucleus, and \( \bar{\nu} \) is a massless neutral particle termed as anti-neutrino. The progeny nucleus has an additional proton and one less neutron that the parent. Therefore, the negatron, form of beta decay results in an increase in \( Z \) of one, a decrease in \( N \) of one, and a constant \( A \).

Negatron decay pathways are characterized by specific maximum energies; however most negatrons are ejected with energies lower than these maxima. The average energy of negatrons is about \( \frac{1}{3} E_{\text{max}} \) along specific pathway.

2.7.3 Positron decay and electron capture

Positron decay results from the nuclear transition

\[
_{1}^{1}p \rightarrow _{-1}^{0}n + _{+1}^{0}\beta + \nu \quad (2.7.3-1)
\]

where \( _{+1}^{0}\beta \) represents a positron ejected from the nucleus during decay, and \( \nu \) is a neutrino that accompanies the positron. The neutrino and antineutrino are similar, except that they have opposite spin and are said to be antiparticles of each other.

In positron decay, the \( n/p \) ratio increases; hence, positron-emitting nuclides tend to be positioned below the \( n/p \) stability curve. Positron decay results in a device of one in \( Z \), an increase of one in \( N \), and no change in \( A \). The \( n/p \) ratio of a nuclide may also be increased by electron capture (ec), in which an electron is captured by the nucleus to yield the transition

\[
_{1}^{1}p+ _{-1}^{0}e \rightarrow _{0}^{1}n + \nu \quad (2.7.3-2)
\]

Most electrons are captured from the K electron shell, although occasionally an electron may be captured from the L shell or a shell even farther from the nucleus. During electron capture, a hole is created in an electron shell deep within the atom. This vacancy filled by an electron cascading from a higher shell, resulting in the release of characteristic radiation or one more Auger electrons.

As mentioned earlier, radioactive decay often forms a progeny nucleus in an energetic (“excited”) state. The nucleus descends from its excited to its most stable (“ground”) energy state by one or more isomeric transitions. Often these transitions occur by emission of electromagnetic radiation termed \( \gamma \) rays. \( \gamma \) rays and x rays occupy the same region of the electromagnetic energy spectrum, and they are differentiated only by their origin: x rays result from electron interactions outside the nucleus, whereas \( \gamma \) rays result from nuclear transitions.

No radioactive nuclide decays solely by an isomeric transition. Isomeric transitions are always preceded by either electron capture or emission of an \( \alpha \) or \( \beta \) (+ or −) particle. Sometimes one or more of the excited states of a progeny nuclide may exist for a finite lifetime.

An isomeric transition can also occur by interaction of the nucleus with an electron in one of the electron shells. This process is known as internal conversion (IC). When IC happens, the electron is ejected with kinetic energy \( E_{k} \) equal to the energy \( E_{\gamma} \) released by the nucleus, reduced by the binding
energy $E_b$ of the electron.

$$E_k = E_\gamma - E_b \quad (2.7.3-3)$$

The ejected electron is accompanied by x rays and Auger electrons as the extranuclear structure of the atom resumes a stable configuration. The internal conversion coefficient for an electron shell is the ratio of the number of conversion electrons from the shell compared with the number of $\gamma$ rays emitted by the nucleus. The probability of internal conversion increases rapidly with increasing $Z$ and with the lifetime of the excited state of the nucleus.

### 2.8 Interaction of Radiation with Matter

When high-energy radiation interacts with matter energy can be transferred to the material. A number of effects may follow, but a common outcome is the ionisation or excitation of the atoms in the absorbing material. In general, the larger the mass of the particle the greater the chance of being absorbed by the material. Large particles such as alpha particles have a relatively short range in matter, whereas beta particles are more penetrating. The extremely small mass of the neutrino, and the fact that it has no charge, means that it interacts poorly with material, and is very hard to stop or detect. High-energy photons, being massless, are highly penetrating.

#### 2.8.1 Interaction of Particle Radiation with Matter

When higher energy particles such as alphas, betas, protons, or deuterons interact with atoms in an absorbing material the predominant site of interaction is with the orbital electrons of the absorber atoms. This leads to ionisation of the atom, and liberation of excited electrons by the transfer of energy in the interaction. The liberated electrons themselves may have sufficient energy to cause further ionisation of neighboring atoms and the electrons liberated from these subsequent interactions are

---

*Figure 2: Graphical representation of a β- decay*
referred to as delta rays. Positron annihilation is an example of a particulate radiation interacting with matter. We have already examined this process in detail.

2.8.2 Interaction of Photons with Matter

High-energy photons interact with matter by three main mechanisms, depending on the energy of the electromagnetic radiation. These are (i) the photoelectric effect, (ii) the Compton effect, and (iii) pair production. In addition, there are other mechanisms such as coherent (Rayleigh) scattering, an interaction between a photon and a whole atom which predominates at energies less than 50 keV; triplet production and photonuclear reactions, where high energy gamma rays induce decay in the nucleus, and which require energies of greater than ~10 MeV. We will focus on the three main mechanisms which dominate in the energies of interest in imaging in nuclear medicine.

2.8.2.1 Photoelectric Effect

The photoelectric effect occupies a special place in the development of the theory of radiation. During the course of experiments which demonstrated that light acted as a wave, Hertz and his student Hallwachs showed that the effect of an electric spark being induced in a circuit due to changes in a nearby circuit could be enhanced if light was shone upon the gap between the two coil ends. They went on to show that a negatively charged sheet of zinc could eject negative charges if light was shone upon the plate. Philipp Lenard demonstrated in 1899 that the light caused the metal to emit electrons. This phenomenon was called the photoelectric effect. These experiments showed that the electric current induced by the ejected electrons was directly proportional to the intensity of the light. The interesting aspect of this phenomenon was that there appeared to be a light intensity threshold below which no current was produced. This was difficult to explain based on a continuous wave theory of light. It was these observations that led Einstein to propose the quantized theory of the electromagnetic radiation in 1905, for which he received the Nobel Prize. The photoelectric effect is an interaction of photons with orbital electrons in an atom. The photon transfers all of its energy to the electron. Some of the energy is used to overcome the binding energy of the electron, and the remaining energy is transferred to the electron in the form of kinetic energy. The photoelectric effect usually occurs with an inner shell electron. As the electron is ejected from the atom (causing ionisation of the atom) a more loosely bound outer orbital electron drops down to occupy the vacancy. In doing so it will emit radiation itself due to the differences in the binding energy for the different electron levels. This is a characteristic X-ray. The ejected electron is known as a photoelectron. Alternately, instead of emitting an X-ray, the atom may emit a second electron to remove the energy and this electron is known as an Auger electron. This leaves the atom doubly charged. Characteristic X-rays and Auger electrons are used to identify materials using spectroscopic methods based on the properties of the emitted particles.

The photoelectric effect dominates in human tissue at energies less than approximately 100 keV. It is of particular significance for X-ray imaging, and for imaging with low-energy radionuclides. It has little impact at the energy of annihilation radiation (511 keV), but with the development of combined

![Figure 3: Graphical representation of photoelectric effect](image-url)
PET/CT systems, where the CT system is used for attenuation correction of the PET data, knowledge of
the physics of interaction via the photoelectric effect is extremely important when adjusting the
attenuation factors from the X-ray CT to the values appropriate for 511 keV radiation.

2.8.2.2 Compton Scattering

Compton scattering is the interaction between a photon and a loosely bound orbital electron. The electron is so loosely connected to the atom that it can be considered to be essentially free. This effect dominates in human tissue at energies above approximately 100 keV and less than ~2 MeV. The binding potential of the electron to the atom is extremely small compared with the energy of the photon, such that it can be considered to be negligible in the calculation. After the interaction, the photon undergoes a change in direction and the electron is ejected from the atom. The energy loss by the photon is divided between the small binding energy of the energy level and the kinetic energy imparted to the Compton recoil electron. The energy transferred does not depend on the properties of the material or its electron density (Fig. 2.10). The energy of the photon after the Compton scattering can be calculated from the Compton equation:

\[ E'_\gamma = \frac{E_\gamma}{1 + \frac{E_\gamma}{m_e c^2} (1 - \cos(\theta_\gamma))} \]  

(2.8.2.2-1)

2.8.2.3 Pair production

The final main mechanism for photons to interact with matter is by pair production. When photons with energy greater than 1.022 MeV (twice the energy equivalent to the rest mass of an electron) pass in the vicinity of a nucleus it is possible that they will spontaneously convert to two electrons with opposed signs to conserve charge. This direct electron pair production in the Coulomb field of a nucleus is the dominant interaction mechanism at high energies. Above the threshold of 1.022 MeV, the probability of pair production increases as energy increases. At 10 MeV, this probability is about 60%. Any energy left over after the production of the electron–positron pair is shared between the particles as kinetic energy, with the positron having slightly higher kinetic energy than the electron as the interaction of the particles with the nucleus causes an acceleration of the positron and deceleration of the electron.

Pair production was first observed by Anderson using cloud chambers in the upper atmosphere, where high-energy cosmic radiation produced tracks of diverging ionisation left by the electron–positron pair. The process of pair production demonstrates a number of conservation laws. Energy is conserved in the process as any residual energy from the photon left over after the electron pair is produced (given by \( E_\gamma - 2m_0 c^2 \)) is carried away by the particles as kinetic energy; charge is conserved as the incoming photon has zero charge and the outgoing positive and negative electrons have equal
and opposite charge; and momentum is conserved as the relatively massive nucleus absorbs momentum without appreciably changing its energy balance. Electron–positron pair production offered the first experimental evidence of Dirac’s postulated “antimatter”, i.e., that for every particle in the universe there exists a “mirror image” version of it. Other particles can produce matter/antimatter pairs, such as protons, but, as the mass of the electron is much less than a proton, a photon of lower energy is required for electron–positron pair production, thus making the process more probable. The particles produced will behave like any other free electron and positron, causing ionisation of other atoms, and the positron will annihilate with an orbital electron, producing annihilation radiation as a result. At energies above four rest–mass equivalents of the electron, pair production can take place in the vicinity of an electron. In this case it is referred to as “triplet production” as there is a third member of the interaction, he recoiling electron.

2.9 Attenuation and Scattering of Photons

In the previous section we have seen how radiation interacts with matter at an atomic level. In this section we will examine the bulk “macroscopic” aspects of the interaction of radiation with matter, with particular reference to positron emission and detection. Calculations of photon interactions are given in terms of atomic cross sections ($\sigma$) with units of $\text{cm}^2$/atom. An alternative unit, often employed, is to quote the cross section for interaction in barns/atom (b/atom) where 1 barn = $10^{-24}$ cm$^2$. The total atomic cross section is given by the sum of the cross sections for all of the individual processes, i.e.,

$$\sigma_{\text{tot}} = \sigma_{\text{pe}} + \sigma_{\text{incoh}} + \sigma_{\text{coh}} + \sigma_{\text{pair}} + \sigma_{\text{tripl}} + \sigma_{\text{nph}} \quad (2.9-1)$$

where the cross sections are for the photoelectric effect (pe), incoherent Compton scattering (incoh), coherent, Rayleigh, scattering (coh), pair production (pair), triplet production (tripl), and nuclear photoabsorption (nph). Values for attenuation coefficient are often given as mass attenuation coefficients ($\mu/\rho$) with units of $\text{cm}^2$.g$^{-1}$. The reason for this is that this value can be converted into a linear attenuation coefficient ($\mu_1$) for any material simply by multiplying by the density ($\rho$) of the material:

$$\mu_1(\text{cm}^{-1}) = \mu/\rho \ (\text{cm}^2\cdot\text{g}^{-1})\rho(\text{g}\cdot\text{cm}^{-3}) \quad (2.9-2)$$

![Figure 5: Probability that a specific type of interaction will take place over the photon energy](image)
2.9.1.1 Photon Attenuation

We have seen that the primary mechanism for photon interaction with matter at energies around 0.5 MeV is by a Compton interaction. The result of this form of interaction is that the primary photon changes direction (i.e., is “scattered”) and loses energy. In addition, the atom where the interaction occurred is ionized. For a well-collimated source of photons and detector, attenuation takes the form of a mono-exponential function, i.e.,

\[ I_x = I_0 e^{-\mu x} \]  \hspace{1cm} (2.9.1.1-1)

where \( I \) represents the photon beam intensity, the subscripts “0” and “x” refer respectively to the unattenuated beam intensity and the intensity measured through a thickness of material of thickness \( x \), and \( \mu \) refers to the attenuation coefficient of the material (units: cm\(^{-1} \)). Attenuation is a function of the photon energy and the electron density (Z number) of the attenuator. The attenuation coefficient is a measure of the probability that a photon will be attenuated by a unit length of the medium. The situation of a well collimated source and detector are referred to as narrow-beam conditions.

However, when dealing with in vivo imaging we do not have a well-collimated source, but rather a source emitting photons in all directions. Under these uncollimated, broad-beam conditions, photons whose original emission direction would have taken them out of the acceptance angle of the detector may be scattered such that they are counted.

In the broad-beam case, an uncollimated source emitting photons in all directions contributes both unscattered and scattered events to the measurement by the detector. In this case the detector “sees” more photons than would be expected if unscattered events were excluded, and thus the transmission rate is higher than anticipated (or, conversely, attenuation appears lower). In the narrow-beam case, scattered photons are precluded from the measurement and thus the transmission measured reflects the bulk attenuating properties of the object alone. The geometry of scattered events is very different for PET and single photon emission computed tomography (SPECT). As PET uses coincidence detection, the line-of-sight ascribed to an event is determined by the paths taken by both annihilation photons. In this case, events can be assigned to lines of response outside of the object. This is not true in the single-photon case where, assuming negligible scattering in air, the events scattered within the object will be contained within the object boundaries.
Chapter's References

[4]. Technology of Nuclear Medicine, prof. I Kandarakis.
3 Positron Emission Tomography Engineering

3.1 Introduction to PET

PET is based on the “Annihilation Coincidence Detection” (ACD) of the two collinear 511 keV γ-photons resulting from the annihilation of a positron (e⁺) and a electron (e⁻) (Fig. 6). Positrons are the antiparticles of electrons, see chapter for high energy physics. Positrons, like every antiparticle, is very short living. Positron-electron annihilation occurs at the end of the positron range, which is when the positron has dispatched most of its kinetic energy thus both the positron and electron are essentially at rest. The total positron and electron energy is therefore 1.22 MeV, the sum of their equal rest mass energies Δm=511 keV (Fig.6), and their total momentum (a vector or signed, quantity) is zero (because they don't have, anymore, any kinetic energy). Accordingly, to conserve energy and momentum, the total energy of the two annihilation γ-photons must equal 1.22 MeV and their total momentum zero.

Therefore are emitted two equal-energy (511 keV) annihilation γ-photons traveling on the same line, in opposite directions; corresponding to equal magnitude, opposite-sign (positive and negative) momenta. In the parlance of ACD, each of the two annihilation photons is referred to as a “single” and the total count rate “counts per second (cps)” for the individual annihilation photons is called the “singles count rate”. Only when signals from the two opposite detectors simultaneously trigger the coincidence circuit a “true coincidence event”, “true”, is generated by this circuit, this logic response is named AND logic (Fig.6). Because various delays are introduced in the system usually but simultaneity is defined by a very narrow timing windows, with width of nsec.

The volume between the opposed coincidence detectors (the shaded area in Fig.6) is referred to as a “line of response (LOR).” LORs are thus defined electronically, and an important advantage of ACD is that absorptive collimator is not required. As a result, the sensitivity (measured as counts rate per unit of activity) of PET is much higher (two to three orders of magnitude higher) than that of SPECT camera imaging. Not every annihilation yields a counted event, because both annihilation photons must strike the coincident detectors for an event to be counted. As a result, the singles count rate in PET is typically much higher than the trues count rate.

Figure 6: Graphical representation of a typical PET system
The energy of 511 keV and the simultaneity of detection requirements for counting of a true coincidence event are not absolute. Scintillation detectors typically have a rather coarse energy resolution up to ~30%, expressed as the percent full-width half-maximum (FWHM) of the 511 keV photopeak and therefore photons within a broad channel range (e.g., from channel 250 to 650) may be counted as valid annihilation events. The “channels” are bins in which the detected γ-photons are sorted. Because before the energy calibration of the camera, the energy response is unknown, we don't know where to sort the detected energy of each γ-photon. Compton-scattered annihilation γ-photons, scattered and unscattered non annihilation γ-photons may therefore be included, producing spurious or mispositioned coincidence events (Fig.7).

Each detected photon, single, is time-stamped, and true coincidence events are defined as a pair of annihilation photons counted by the coincidence detectors within a time interval called the “coincidence timing window” or just “acceptance window”, which typically is 6 to 12 nsec wide (Fig.6). Such a finite timing window is necessitated by several considerations:

➢ First, depending on the exact position of the positron-electron annihilation, the γ-photons reach the detectors at slightly different times. However, because these photons travel at the speed of light (c =3x10^10 cm/s), this effect is very small. A new technique currently is being developed on this effect (see Time-Of-Flight (TOF) technique).

➢ Second, the transit and processing of the signal pulses through the detector circuitry is rapid but not instantaneous.

➢ Third, the light signal emitted by the scintillation detectors used in PET is emitted not instantaneously but over a finite time interval, called the “scintillation decay time” of the order of 10 to 100 nsec.

In addition to the true coincidence events, a number of other types of events occur in PET, events that degrade quantitative accuracy as well as image quality. Random or accidental coincidence events “randoms” occur when annihilation γ-photons from two separate positron-electron annihilations are detected in two different detectors within the coincidence timing window (Fig.7.B). Randoms thus increase the detected coincidence count rate by contributing spuriously placed coincidence events. Because the total volume containing the isotope is typically much greater than the LOR, random coincidences are common and the randoms count rate may actually exceed the trues count rate. Clinically, the ratio of the randoms to true count rates range from 0.1 to 0.2 for brain imaging to greater than 1 for whole body imaging. The randoms count rate is actually proportional to the product of the singles count rate and therefore the square of the activity present:

\[ C_{\text{randoms}} = 2\tau C_1 C_2 \]  (3.1-1)

where \( C_{\text{randoms}} \) are the randoms count rate (cps) (Fig.7B), \( \tau \) the coincidence timing window (sec), and \( C_1 \) and \( C_2 \) are the detector 1 and detector 2 singles count rates (cps), respectively (Fig.6, Fig.7A). Importantly, because the trues count rate is linearly proportional to the activity, the ratio of the randoms to trues count rates increases linearly with activity. Therefore, imaging times cannot be reduced simply by using higher administered activities, as the randoms count rate will increase faster than the trues count rate and at some point prohibitively degrade image quality. By using absorptive septa to restrict the region, which contains the isotope, to a volume defined by the cross-sectional area of side by side detectors as in two-dimensional (2D) PET (see next paragraph) the randoms to true count rate ratio can be reduced substantially. By using “faster” detectors and therefore shorter coincidence timing windows, the randoms to true count rate can be further reduced (see below).

Annihilation γ-photons traveling out of an LOR may undergo Compton scatter and be redirected back into the LOR (Fig.5C). The scattered photon, however, may retain sufficient energy to fall within the energy window set for the 511 keV annihilation γ-photons and produce a coincidence event. Such scatter coincidences “scatter” result in mispositioned events. The scatter count rate as well
as the trues count rate are proportional to the activity present and therefore the scatter to trues count rate ratio is independent of activity. Because trues and scatter each result from single annihilation events, the scatter to trues count rate ratio is likewise independent of the coincidence timing window. On the other hand, interdetector septa used in 2D PET reduce the scatter count rate considerably.

Many positron emitting radioisotopes also emit significant numbers of high energy prompt γ photons, and such γ-photons may be in cascade with each other or with the positrons. These can result in spurious coincidences which are spatially uncorrelated but nonetheless counted as true events (Fig 2D). Although such coincidences degrade overall quality and quantitative accuracy, isotopes such as those in Table 1 have been used effectively in PET. Besides the γ-photons energies and abundance, Table 1 includes other pertinent properties of positron emitters such as the physical half-life ($T_{1/2}$), the branching ratio (ie, the percentage of total decays resulting in positron emission instead of electron capture), the maximum positron energies ($E_{max}$), the maximum extrapolated range ($R_{max}$), the root-mean-square ($rms$) positron range ($R_{rms}$), and the method of production.

**Table 1.** Isotopes used in PET imaging, clinically or experimental and their major properties.

<table>
<thead>
<tr>
<th>Isotope</th>
<th>$T_{1/2}$</th>
<th>Branching Ratio(%)</th>
<th>$β^+ E_{max}$ (MeV)</th>
<th>$β^+$ range in water</th>
<th>Production</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>$R_e$</td>
<td>$R_{rms}$</td>
</tr>
<tr>
<td>Carbon-11</td>
<td>99</td>
<td>0.96</td>
<td>3.9</td>
<td>0.4</td>
<td>Cyclotron</td>
</tr>
<tr>
<td>Nitrogen-13</td>
<td>100</td>
<td>1.2</td>
<td>5.1</td>
<td>0.6</td>
<td>Cyclotron</td>
</tr>
<tr>
<td>Oxygen-15</td>
<td>100</td>
<td>1.7</td>
<td>8.0</td>
<td>0.9</td>
<td>Cyclotron</td>
</tr>
<tr>
<td>Fluorine-18</td>
<td>97</td>
<td>0.64</td>
<td>2.3</td>
<td>0.2</td>
<td>Cyclotron</td>
</tr>
<tr>
<td>Copper-62</td>
<td>98</td>
<td>2.9</td>
<td>15</td>
<td>1.6</td>
<td>Generator (Zinc-62)</td>
</tr>
<tr>
<td></td>
<td>19</td>
<td>0.58</td>
<td>2.0</td>
<td>0.2</td>
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<tr>
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<td>----</td>
<td>------</td>
<td>-----</td>
<td>-----</td>
<td>------------</td>
</tr>
<tr>
<td>Copper-64</td>
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<td></td>
<td>Cyclotron</td>
</tr>
<tr>
<td>Gallium-66</td>
<td>56</td>
<td>3.8</td>
<td>20</td>
<td>3.3</td>
<td>Cyclotron</td>
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<tr>
<td>Gallium-68</td>
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<td>9.0</td>
<td>1.2</td>
<td>Generator (Ge-68)</td>
</tr>
<tr>
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<td>3.2</td>
<td>Cyclotron</td>
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<tr>
<td>Rubidium-82</td>
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<td>2.6</td>
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<td>Cyclotron</td>
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<tr>
<td>Iodine-124</td>
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<td>1.5</td>
<td>7.0</td>
<td>0.8</td>
<td>Cyclotron</td>
</tr>
</tbody>
</table>

### 3.2 Detector Types

Radiation detectors can generally be divided into three broad categories: proportional (gas) chambers, semiconductor detectors, and scintillation detectors.

1. The *proportional chamber* works on the principle of detecting the ionisation produced by radiation as it passes through a gas chamber. A high electric field is applied within this chamber that results in an acceleration of the ionisation electrons produced by the radiation. Subsequently, these highly energetic electrons collide with the neutral gas atoms resulting in secondary ionisations. Hence, a cascade of electrons is eventually collected at the cathode after some energy deposition by the incident radiation. Typically, inert gases such as xenon are used for detecting photons. The cathode normally consists of a single thin wire, but a fine grid of wires can be utilized to measure energy deposition as a function of position within the detector. Such position-sensitive *Multi-wire Proportional Chambers (MWPC)* have been used in high energy physics for a long time, and PET scanners have been developed based upon such a detector. However, the disadvantage of these detectors for use in PET is the low density of the gas, leading to a reduced stopping efficiency for 511 keV photons, as well as poor energy resolution.

2. Another class of radiation detectors is the *semiconductor* or *solid-state* detectors. In these detectors, incident radiation causes excitation of tightly bound (valence band) electrons such that they are free to migrate within the crystal (conduction band). An applied electric field will then result in a flow of charge through the detector after the initial energy deposition by the photons. Semiconductor detectors have excellent energy resolution but because of their production process, the stopping efficiency for 511 keV photons is low.

3. The third category of radiation detectors, which are of most interest to us, are the *scintillation detectors*. These detectors consist of an inorganic crystal (scintillator) which emits visible (scintillation) light photons after the interaction of photons within the detector. A photo-detector is used to detect and measure the number of scintillation optical photons emitted by an interaction. The number of scintillation photons (or intensity of light) is generally proportional to the energy deposited within the crystal. Due to their high atomic numbers and therefore density, scintillation detectors provide the highest stopping efficiency for 511 keV photons. The energy resolution and the spatial resolution, though much better than the proportional chambers, is not as good as that attained with the semiconductor detectors. This is due to the inefficient process of converting deposited energy into scintillation photons, the subsequent detection by the photo-detectors as well as the spread of the optical photons, described by the law of Swank. However, for PET, where both high stopping efficiency as well as good energy resolution are desired, scintillation detectors are most commonly used. *(The system we will evaluated has a scintillation detector by LSO crystal, thus the thesis include only the description only of this*
3.2.1 Scintillation Process

The electronic energy states of an isolated atom consist of discrete levels as given by the Schrödinger equation. In a crystal lattice, the outer levels are perturbed by mutual interactions between the atoms or ions, and so the levels become broadened into a series of allowed bands. The bands within this series are separated from each other by the forbidden bands. Electrons are not allowed to fill any of these forbidden bands. The last filled band is labelled the valence band, while the first unfilled band is called the conduction band. The energy gap, $E_g$, between these two bands is a few electron volts in magnitude (Fig. 8).

Electrons in the valence band can absorb energy by the interaction of the photoelectron or the Compton scatter electron with an atom, and get excited into the conduction band. Since this is not the ground state, the electron de-excites by releasing scintillation photons and returns to its ground state. Normally, the value of $E_g$ is such that the scintillation is in the ultraviolet range. By adding impurities to a pure crystal, such as adding thallium ($Tl$) to pure NaI (at a concentration of ~1%), the band structure can be modified to produce energy levels in the prior forbidden region. Adding an impurity or an activator raises the ground state of the electrons present at the impurity sites to slightly above the valence band, and also produces excited states that are slightly lower than the conduction band. Keeping the amount of activator low also minimizes the self-absorption of the scintillation photons. The scintillation process now results in the emission of visible light that can be detected by an appropriate photo-detector at room temperature. Such a scintillation process is often referred to as luminescence. The scintillation photons produced by luminescence are emitted isotropically from the point of interaction. For thallium-activated sodium iodide (NaI:Tl), the wavelength of the maximum scintillation emission is 415 nm, and the photon emission rate has an exponential distribution with a decay time of 230 nsec. Sometimes the excited electron may undergo a radiation-less transition to the ground state. No scintillation photons are emitted here and the process is called quenching.

There are four main properties of a scintillator which are crucial for its application in a PET detector. These are:

- **The stopping power for 511 keV photons.** Which is characterized by the mean distance (attenuation length = $1/\mu$) travelled by the photon before it deposits its energy within the crystal. For a PET scanner with high sensitivity, it is desirable to maximize the number of photons which interact and deposit energy in the detector. Thus, a scintillator with a short attenuation length will provide maximum efficiency in stopping the 511 keV photons. The attenuation length of a scintillator depends upon its density ($\rho$) and the effective atomic number ($Z_{eff}$) of the material.

- **Signal decay time.** The decay constant affects the timing characteristics of the scanner. A short decay time is desirable to process each pulse individually at high counting rates, as well as to reduce the number of random coincidence events occurring within the scanner geometry.

- **Light output.** A high light-output scintillator affects a PET detector design in two ways: it helps achieve good spatial resolution with a high encoding ratio (ratio of number of resolution elements, or crystals, to number of photo-detectors) and attain good energy resolution. Good energy resolution is needed to efficiently reject events which may Compton scatter in the patient before entering the detector.
The intrinsic energy resolution. The energy resolution \((\Delta E/E)\) achieved by a PET detector is dependent not only upon the scintillator light output but also the intrinsic energy resolution of the scintillator. The intrinsic energy resolution of a scintillator arises due to inhomogeneities in the crystal growth process as well as non-uniform light output for interactions within it. Table 2 has the most common scintillators used in PET detectors and their main properties.

### 3.2.2 Detectors and Detector Configurations

Generally, the photo-detectors used in scintillation detectors for PET can be divided into two categories, the *photo-multiplier tubes (PMTs)* and the semiconductor based *photodiodes* (in this thesis only the PSPMT will be describable and analysed as is the detector of our PET camera).

Photomultiplier tubes ([Fig.9](#)) represent the oldest and most reliable technique to measure and detect low levels of scintillation light. They consist of a vacuum enclosure with a thin photocathode layer at the entrance window. An incoming scintillation photon deposits its energy at the photocathode and triggers the release of a photoelectron. Depending upon its energy, the photoelectron can escape the surface potential of the photo-cathode and in the presence of an applied electric field accelerate to a nearby dynode which is at a positive potential with respect to the photocathode. Upon impact with the dynode, the electron, with its increased energy, will result in the emission of multiple secondary electrons. The process of acceleration and emission is then repeated through several dynode structures lying at increasing potentials, leading to a gain of more than a million at the final dynode (anode). This high gain obtained from a photomultiplier tube leads to a very good signal to noise ratio (SNR) for low light levels and is the primary reason for the success and applicability of photo-multiplier tubes for use in scintillation detectors. The only drawback of a PMT is the low efficiency in the emission and escape of a photoelectron from the cathode after the deposition of energy by a single scintillation photon. This property is called the *Quantum Efficiency (QE)* of the photomultiplier tube and it is typically \(~25\%\) for most of the photomultiplier tubes. Different, complex arrangements of the dynode structure have been developed over the years in order to maximize the gain, reduce the travel time of the electrons from the cathode to the anode and between each dynode, as well as reduce the variation in the travel times of individual electrons. In particular, a fine grid dynode structure has been developed which restricts the spread of photoelectrons while in trajectory, thereby providing a position-sensitive energy measurement within a single photomultiplier tube enclosure (*Position Sensitive PMT* or *PS-PMT*). More recently, a multichannel capability has been developed which essentially reduces a single photomultiplier tube enclosure into several very small channels. It uses a 2D array of glass capillary dynodes each of which is a few microns wide. Additionally, a multi-anode structure is used for electron collection, thereby providing a dramatically improved position sensitive energy measurement with very little cross talk between adjacent channels (*Multi-Channel PMT, MC-PMT*).
In general, there are three ways of arranging the scintillation crystals and coupling them to photo-detectors for signal readout in a PET detector.

The first is the one-to-one coupling, where a single crystal is glued to an individual photodetector. A close-packed array of small discrete detectors can then be used as a large detector that is needed for PET imaging. The spatial resolution of such a detector is limited by the size of the discrete crystals making up the detector. In order to achieve spatial resolution better than 4 mm in one-to-one coupling, very small photo-detectors are needed. However, individual photomultiplier tubes of this size are not currently manufactured. One solution is the use of photodiodes, or APDs instead of photomultiplier tubes. The APDs are normally developed either as individual components or in an array, and so are ideal for use in such a detector design. However, as mentioned earlier, the APD gain is sensitive to variations in temperature and bias voltage that can lead to practical problems of stability in their implementation for a complete PET scanner. Another option is the coupling of individual channels of a PS-PMT or a MC-PMT to the small crystals. Due to the large package size of these photomultiplier tubes, however, clever techniques are needed to achieve a close-packed arrangement of the crystals in the scanner design. Despite the very good spatial resolution and minimal dead time achieved by the one to one coupling design, the inherent complexity (number of electronic channels) and cost of such PET detectors limits their use at present to research systems; in particular, small animal systems or dedicated PET systems.

The next two detector schemes are attempts at reducing these disadvantages by increasing the encoding for the detector. Both the designs involve the use of larger photomultiplier tubes without intrinsic position sensing capabilities. The Anger detector, originally developed by Hal Anger in the 50's, uses a large (e.g., 1 cm thick x 30–50 cm in diameter) \( \text{NaI}:Tl \) crystal glued to an array of photomultiplier tubes via a light guide. This camera is normally used with a collimator to detect low energy single photons in SPECT imaging. An application of the Anger technique to a PET detector, on the other hand, uses 2.5 cm thick \( \text{NaI}:Tl \) scintillators. An array of 6.5 cm diameter photomultiplier tubes can be used to achieve a spatial resolution of about 5 mm. A weighted centroid positioning algorithm is used for estimation of the interaction position within the detector. This algorithm uses a weighted sum of the individual photomultiplier tube signals and normalizes it with the total signal obtained from all the photomultiplier tubes. The weights for the photomultiplier tube signals depend exclusively upon the photomultiplier tube position within the array. Since these detectors involve significant light sharing between photomultiplier tubes, a high light output scintillator such as \( \text{NaI}:Tl \) is needed to obtain good

\[ \text{Figure 9: A graphical representation of a typical PMT. (obtained from the Hamamatsu PMT guide)} \]
spatial resolution. The use of large photomultiplier tubes produces a very high encoding ratio, leading to a simple and cost effective design. However, a disadvantage of this detector, independent of the use of NaI:Tl as a scintillator, is the spread of scintillation light within the crystal which leads to significant detector dead time at high count rates.

3.3 PET Detector Schemes

Most commonly in dedicated PET scanners, detectors are arranged in rings or polygonal arrays of discrete, small-area detectors completely encircling the patient (Fig.10, Fig.11A–B-C). In such systems, multi-coincidence fan beam detection is used (Fig.10), with each detector element operated in coincidence with multiple opposed detector elements. For a ring comprised of \(N\) detector elements, a total of \(N/4\) to \(N/2\) fan beams is acquired. In rings, each element is typically in coincidence with about half of the total detectors in the ring and in polygonal arrays with the opposed detector bank. PET systems with only partial detector rings are less expensive but require rotation of the detector assembly about the longitudinal axis of the patient to complete acquisition of the projection data (Fig 5.D-E). Technical performance improves but cost increases as one progresses from dual-head coincidence Anger cameras at the low end to partial rings to polygonal arrays to multiple full rings at the high end multiple rings being the prevailing configuration among current dedicated PET scanners.

Early PET detectors consisted of a single scintillation crystal backed by a single PMT, with the cross-sectional dimensions of the crystal defining the coincidence LOR and thus intrinsic (i.e., crystal) spatial resolution. To improve spatial resolution, therefore, greater numbers of smaller crystals are required. Thus, the practically achievable miniaturization of PMTs and
associated electronics and the cost of large numbers of detectors, PMTs, etc, representing well over half of the costs of PET scanners, limit intrinsic resolution. The block detector was the solution to this limitation. A block detector consists of a large cubic piece of scintillator (2x2 to 3x3 cm in cross section by 2 to 3 cm in depth) partially cut, or scored, depth-wise into a rectangular array of detector elements (Fig 12.A). The cuts are filled with reflective material to optically isolate the detector elements from one another and to maximize light collection efficiency by the PMTs backing the scintillator. Crystal elements with a somewhat smaller cross-section improve spatial resolution but only to a certain point.

As the cross-section of detector elements is reduced and the number of elements increased, the number of cuts and therefore the fraction of the scintillator face occupied by the filling material increase. As a result, the detector element packing fraction (i.e., the fraction of the scintillator face occupied by scintillation material) and therefore the intrinsic sensitivity decrease.

The depth of the cuts into the crystal is not uniform but increases from approximately half the thickness at the center to nearly the full thickness at the edge of each side of the scintillator (Fig.12.A); the actual depths of the cuts are determined empirically to yield a spatially linear distribution of light among the four PSPMTs, in a 2x2 array, backing the scintillator. The position at which the annihilation $\gamma$-photons strike the scintillator is then determined by Anger logic.

The response of the block detector is not uniform (Fig.12.B). Rather, recorded events are clustered at points corresponding to the individual detector elements and then assigned to a specific element in the 2D array using a look-up table (LUT) derived by uniform irradiation of the scintillator. The major advantage of the block detector is that it allows an array of many small detector elements 8x8 to be spatially encoded using only four PMTs rather than one PMT per element, yielding high spatial resolution while minimizing costs.

In modern multi ring detector PET scanners there are typically three to four rings of 100 to 200 block detectors each. There are about 6 to 8 cuts per block detector, yielding an array of 6x6 to 8x8 elements 4x4 to 6x6 mm each. Overall, therefore, there are a total of 10,000 to 20,000 detector elements. Ring diameters range from 80 to 90 cm, the patient ports and transaxial fields of view from 50 to 70 cm, and the axial (or longitudinal) fields of view from 20 to 30 cm, typically yielding about 50 transaxial image planes each 2 to 4 mm thick.

An important refinement of the block detector is the “quadrant (or light) sharing”; where a two by two array of four larger PMTs not only backs a single scintillator block but each PMT in the array also backs the corner of an adjacent block. This reduces the total number of PSPMTs by a factor of four and thus reduces overall cost. Disadvantages of quadrant sharing include higher dead time count losses and more involved detector servicing because of the non modular design (Fig.13).

A notable refinement of PET scintillators has been the use of adjacent layers of two different materials with significantly different scintillation decay times (such as LSO and GSO, with decay times of approximately 40 and 60 nsec, respectively); this is known as phoswich.

Based on the pulse shape of the scintillation signal, the interaction of the annihilation $\gamma$-photon can therefore be localized to one or the other half of the phoswich detector. The resolution degrading depth-of-interaction effect is therefore reduced by a factor of two. However, the fabrication of phoswich is more complex than that of single component detectors, and to date it has not been widely used in commercial PET scanners.

A new method for further improvement of the performance of the PET detector is the “Time of
Flight” method (TOF). TOF PET technology is based on the measurement of the actual time difference between the detection of two coincident gamma rays originating from the same annihilation process. This time difference is then used to reduce noise in image data, resulting in higher image quality, shorter imaging times or a lower dose to the patient. The TOF PET scanner concept is more than 25 years old but has remained undeveloped owing to the lack of crystals with high light output (bright) and short decay time (fast). The results showed that contrast recovery improves slightly with TOF, and that improved timing resolution leads to a faster convergence to the maximum contrast value. Detectability for 10 mm diameter hot spheres estimated using a non-prewhitening matched filter (NPW SNR) also improved non-linearly with TOF. The gain in image quality using contrast and noise measures was proportional to the object diameter and inversely proportional to the timing resolution of the scanner. The gains in NPW SNR were smaller, but they also increased with increasing object diameter and improved timing resolution. The results show that scan times can be reduced in a TOF scanner to achieve images similar to those from a non-TOF scanner, or that improved image quality can be achieved for the same scan times.

3.4 2D Versus 3D Imaging

PET ring scanners originally employed lead or tungsten walls, or septa, positioned between and extending radially inward from the detector elements (Figs 14.A-C, Fig.15). In this approach, known as 2D PET, these interring annular septa define plane by plane LORs and largely eliminate out of plane annihilation $\gamma$-photons. By minimizing the contribution of out of plane randoms and scatter, image quality is optimized, especially for large volume sources (i.e. as in whole-body PET). However, 2D PET also eliminates most trues and thus reduces sensitivity considerably.

Typically, both “direct” and “cross” image planes are reconstructed from LORs within the same detector ring, corresponding to a so called “ring difference ($\Delta$)” of 0, and between two adjacent detector rings (ring difference of $\pm1$), respectively. The cross planes lie halfway between the direct planes defined by detector elements and, conceptually, can be assigned to a “virtual” ring of detectors lying midway between two adjacent detector rings. Because the cross plane images result from two LORs and the direct plane images from only one, the cross plane image sensitivity is about twice that of the direct plane images. This results, in an uncorrected PET study of a uniform volume source, in alternating lower count and higher count transverse section images. In the newer 2D PET systems, LORs among as many as three adjacent rings, corresponding to a ring difference of $\pm3$, are used to improve sensitivity. Increasing the ring difference does, however, degrade spatial resolution somewhat.

Sensitivity can be increased substantially by removing the septa altogether and including coincidence events from all of the LORs among all the detectors (Fig.14.D) a system with 10,000 detector elements has approximately 100 million LORs. This is known as 3D PET and is widely used among, state of the art, PET scanners. “Collimator less” Anger camera-based coincidence imaging of positron emitters is inherently 3D.

Sensitivity is increased approximately five times in 3D relative to 2D PET but with a considerable increase in the randoms and scatter count rates. Clinically, the scatter to true count rate ratios range from 0.2 (2D) to 0.5 (3D) in brain and from 0.4 (2D) to 2 (3D) in the whole body.

To compensate for the increase in scatter count rates, detectors (such as GSO and LSO) with better energy resolution and accurate scatter correction algorithms, are required for 3D PET. And, to minimize the increased randoms count rates and deadtime count rate losses, shorter coincidence timing windows, and therefore faster crystals (such as GSO and LSO), are required. Data processing time, for 3D PET is about an order of magnitude longer than for 2D PET.

In contrast to the relatively uniform axial sensitivity for 2D PET, the axial sensitivity profile for a 3D PET scanner is triangular and peaked at the center of the field of view. Thus, whole body 3D PET studies require considerable overlap of adjacent bed position acquisitions optimally, one half of the
axial FOVs to yield uniform sensitivity over the resulting whole body images.

1.1 PET Performance Characterization

1.1.1 Spatial Resolution

The overall spatial resolution, expressed as the full width at half maximum (FWHM) of the line spread function (LSF), of PET scanners result from a combination of physical and instrumentation factors. There are several important limitations imposed on resolution by the basic physics of positron electron annihilation (Fig.10). First, for a given radionuclide, positrons are emitted over a spectrum of initial kinetic energies ranging from 0 to a characteristic maximum energy, $E_{\text{max}}$. The associated average positron energy, $E_{\text{rms}}$, is approximately one-third of its endpoint energy:

$$E_{\text{rms}} = \frac{1}{3} E_{\text{max}} \quad (3.5.1-1)$$

Positrons will therefore travel a finite distance from the decaying nucleus ranging from 0 to a maximum called the extrapolated range ($R_e$), from 2 to 20 mm, corresponding to its highest energy.

Figure 15: Multiring commercial PET gantry with applied septa.

Figure 14: Schematic representation of possible LORs in 2D (A-C) and 3D (D) acquisition.
positrons, the effective atomic number \((Z_{\text{eff}})\) and the density \((d)\) of the material. For positron emitters used to date in PET, the maximum energies \((E_{\text{max}})\) vary from 0.58 to 3.7 MeV, the extrapolated ranges \((R_e)\) from 2 to 20 mm, and the root mean square \((\text{rms})\) ranges \((R_{\text{rms}})\) from 0.2 to 3.3 mm (Table 1).

Although the finite positron range acts to degrade spatial resolution, the range related blurring is mitigated by the spectral distribution of positron energies for a given radio isotope as well as the characteristically tortuous path positrons travel. These effects are reflected by the fact the \(\text{rms}\) positron ranges are nearly 10 times shorter than the extrapolated positron ranges (Table 1). The perpendicular distance the positron travels is thus considerably shorter than the actual path length it travels (Fig.16). The positron range degrades spatial resolution by only \(\sim 0.1\) mm for Fluorine-18 \((E_{\text{max}}=640\) keV\) and \(\sim 0.5\) mm for Oxygen-15 \((E_{\text{max}}=1720\) keV\). These values are much closer to the respective \(\text{rms}\) positron ranges, 0.2 and 0.9 mm, than to the respective extrapolated positron ranges, \(\sim 2.3\) and \(\sim 8.0\) mm.

The second physics-related limitation on PET performance is the non collinearity of the two annihilation \(\gamma\)-photons. Because a positron actually has some small residual (nonzero) momentum and so some kinetic energy at the end of its range, the two annihilation photons are not emitted exactly back to back, \(180^\circ\) apart, but deviate from collinearity by up to \(\pm 0.25^\circ\). The non collinearity related blurring, \(\text{FWHM}_{180^\circ}\), varies from \(\sim 2\) mm for an 80 cm diameter whole body PET to \(\sim 0.7\) mm for a 30 cm diameter brain PET to \(\sim 0.3\) mm for a 12 cm diameter small-animal PET (Fig.16).

Among instrumentation related determinants of overall spatial resolution are the intrinsic detector resolution and the depth of interaction effect. For discrete, small-area detectors, resolution is determined by the pixel width \((w)\), increasing from \(w/2\) midway between opposed coincidence detectors to \(w\) at the face of either detector. For continuous, large area detectors the intrinsic resolution \((\text{FWHM}_{\text{intrinsic}})\), which is determined empirically, increases from \(\text{FWHM}_{\text{intrinsic}}/\sqrt{2}\) midway between the opposed detectors to \(\text{FWHM}_{\text{intrinsic}}\) at the face of either detector.

For PET systems using rings of discrete, small-area detectors, the depth of the detector elements

---

**Figure 16:** Graphical illustration of the physical PET limitations.
(2-3 cm typical values) results in a degradation of spatial resolution termed the depth-of-interaction (DOI) or parallax effect (Fig.16). With increasing radial offset of a source from the center of a detector ring, the effective detector width and, with it, the intrinsic resolution increase. In whole body PET scanners, the detector depth is typically 2 to 3 cm, the detector width about 4 mm, and the detector ring diameter about 80 cm and the DOI effect thus degrades spatial resolution by 50% at 10 cm from the center of the detector ring.

3.4.1 Sensitivity

System sensitivity (the measured event rate per unit activity) is determined by the combination of geometric efficiency (the fraction of emitted photons striking the detector) and intrinsic efficiency (the ability of the detectors to stop and detect the γ-photons).

The geometric efficiency is equivalent to the fractional solid angle at the source subtended by the detector. For a ring detector of depth \( d \) and diameter \( D \) and ignoring the small interdetector area, the geometric efficiency (\( g \)) decreases linearly from approximately \( d/D \) at the center to 0 at the end of the ring, yielding an average geometric efficiency of \( d/2D \).

Based on the exponential attenuation of radiation, the monochromatic intrinsic efficiency (\( \epsilon \)) is given by \( 1-e^{-\mu d} \), where is the linear attenuation coefficient \( \mu (\text{cm}^{-1}) \) of the detector material for 511 keV γ-photons and \( d \) is the thickness (cm) of the detector. For coincidence detection of the two 511 keV annihilation γ-photons, the intrinsic efficiency is actually \( \epsilon^2 \). Because of the quadratic dependency on intrinsic sensitivity for ACD, the differential stopping power for 511 keV γ-photons is accentuated: for BGO and LSO, is nearly 50% greater than for GSO and nearly three times greater than for NaI:Tl (Table 2).

Commercial PET system sensitivities, for a point source at the center of the FOV, range from 0.2 to 0.5% (74-185 cps/ Ci) for 2D scanners to 2 to 10% (740-1850 cps/ Ci) for 3D scanners. SPECT system sensitivities, on the other hand, typically have 10 and 100 times lower sensitivities than 2D and 3D PET scanners, respectively.

Table 2. Crystal used in PET detectors.

<table>
<thead>
<tr>
<th>Scintillator</th>
<th>Type</th>
<th>Density (g/cm³)</th>
<th>( Z_{	ext{eff}} )</th>
<th>Linear attenuation coefficient ( \mu (\text{cm}^{-1}) )</th>
<th>Light Yield (Ph/keV)</th>
<th>Emission Wavelength (nm)</th>
<th>Decay time (ns)</th>
<th>Hygroscopic</th>
</tr>
</thead>
<tbody>
<tr>
<td>NaI:Tl</td>
<td>Crystal</td>
<td>3.67</td>
<td>50.6</td>
<td>0.3411</td>
<td>38</td>
<td>415</td>
<td>230</td>
<td>yes</td>
</tr>
<tr>
<td>BGO</td>
<td>Crystal</td>
<td>7.13</td>
<td>75</td>
<td>0.9496</td>
<td>9</td>
<td>480</td>
<td>300</td>
<td>no</td>
</tr>
<tr>
<td>GSO:Ce</td>
<td>Crystal</td>
<td>6.7</td>
<td>59</td>
<td>0.6978</td>
<td>12.5</td>
<td>440</td>
<td>60</td>
<td>no</td>
</tr>
<tr>
<td>LSO:Ce</td>
<td>Crystal</td>
<td>7.4</td>
<td>66</td>
<td>0.8658</td>
<td>27</td>
<td>420</td>
<td>40</td>
<td>no</td>
</tr>
<tr>
<td>YSO</td>
<td>Crystal</td>
<td>4.53</td>
<td>34.2</td>
<td>0.3875</td>
<td>46</td>
<td>420</td>
<td>70</td>
<td>no</td>
</tr>
</tbody>
</table>

3.4.2 Noise-Equivalent Count Rate (NECR)

The “noise-equivalent count rate” (NECR), is a important parameter of practical PET performance, is defined as:

\[
\frac{T^2}{T + S + R}
\]
where $T$, $S$, and $R$ the trues, scatter, and randoms count rates, respectively. The maximum NECR is thus the optimal count rate for a particular scanner. For 2D scanners, the interdetector septa effectively reduce the contribution of the scatter and randoms count rates such that the NECR is essentially equivalent to the trues rate. Thus, for 2D scanners, the NECR increases linearly with activity and there is no optimal count rate or activity. For 3D scanners, on the other hand, the trues and scatter count rates are proportional to the activity while the randoms count rate is proportional to the square of the activity. Thus, there exists a well-defined optimum activity for 3D scanners.

The faster the detectors, and therefore the shorter the coincidence timing window, the lower the randoms count rate for a given activity and the higher the activity at which the maximum NECR occurs and the higher the value of the maximum NECR. A “fast” 3D LSO scanner (coincidence timing window: $6$ nsec) has a maximum NECR several times higher than that of a “slower” 3D BGO scanner (coincidence timing window: $12$ nsec). A fast 3D scanner allows the use of higher administered activities and yields high “usable” count rates, short scan durations, and accelerated patient throughput. At clinical activities (eg, $185$ MBq $5$ mCi to $370$ MBq $10$ mCi of fluorine-18), even “slow” 3D scanners have substantially higher sensitivities and NECRs than 2D scanners.

3.5 Data Processing: Normalizations and Corrections, Image Reconstruction and Quantization

3.5.1 Dead time Correction

PET scanners have a finite dead time and associated count losses. The dead time is the length of time required for a counting system to fully process and record an event, during which additional events cannot be recorded. As a result, the measured count rate is systematically lower than the actual count rate. Such count losses are significant, however, only at “high” count rates, greater than the inverse dead time expressed in seconds. For multidetector ring PET systems, deadtime count losses are generally minimal at clinical administered activities. Nonetheless, a real time correction for deadtime count losses is routinely applied to the measured count rates. Most commonly, this is performed by scaling up the measured count rate, either per LOR or globally, based on an empirically derived mathematical relationship between measured and true count rates.

3.5.2 Randoms Correction

Randoms increase the detected coincidence count rate by contributing spuriously placed coincidence events and thus reduce image contrast and distort the relationship between image intensity and activity concentration. The standard approach to randoms correction, the “delayed window” method, is based on the fact that the random coincidence photons are temporally uncorrelated, not simultaneously emitted. Briefly, once singles in the coincidence timing window (typically $6$-$12$ nsec) are detected, the number of singles in a timing window equal in duration to, but much later ($50$ nsec later) than, the coincidence timing window are determined. The number of events in the delayed timing window provides an estimate of the number of randoms in the coincidence timing window. Real time subtraction of the delayed window counts from the coincidence window counts for each LOR thus corrects for randoms.

3.5.3 Normalization

Even optimally performing PET scanners exhibit some non uniformity of response. Among the $10,000$ to $20,000$ detector elements in a modern ring scanner, slight variations among the detector
elements in thickness, light emission properties, electronics performance etc result in slightly different LOR count rates for the same activity. In principle, nonuniform response can be corrected by acquiring data for a uniform flux of annihilation $\gamma$-photons. If $LOR_T$ is the total number of LORs and a total of $N_T$ events is acquired in the normalization scan, the average number of counts per LOR, $N_{\text{LOR}}$, is simply:

$$N_{\text{LOR}} = \frac{N_T}{LOR_T} \quad (3.6.3-1)$$

For the LOR between detectors $i$ and $j$, $LOR_{ij}$, with measured number of events $N_{ij}$, the normalization factor $NF_{ij}$ is:

$$NF_{ij} = \frac{N_{\text{LOR}}}{N_{ij}} \quad (3.6.3-2)$$

and, for the scan of a patient, the normalized, or corrected, number of events, $C'_{ij}$, in this LOR is:

$$C'_{ij} = NF_{ij} C_{ij} \quad (3.6.3-3)$$

where $C_{ij}$ the raw, or uncorrected, number of events in the LOR between detectors $i$ and $j$.

The normalization scan can be performed using a positron emitting rod source (e.g., germanium-68) spanning the entire axial FOV and rotating it around the periphery of the FOV, exposing the detector pairs to a uniform photon flux per revolution. Alternatively, a uniform cylinder of a positron emitting radionuclide can be scanned and the data thus acquired analytically corrected for attenuation; for a well defined geometry such as a uniform cylindrical source, this correction is straightforward. However, for 3D PET, the contribution of, and correction for, scatter with such a large volume source are not trivial. In practice, either approach is somewhat problematic because of statistical considerations. With approximately 10,000 detector elements and 100 million LORs in a 3D PET scanner, even at a count rate of one million cps it would take several days to acquire a sufficient number of counts per LOR, for example 10,000, required to reduce the statistical uncertainty per LOR normalization factor to 1%. Alternatively, therefore, the response per detector, rather than per LOR, can be measured and the LOR normalization factors then calculated. This would require 10,000 times fewer counts to achieve the same statistical uncertainty, 1%, as required by direct measurement of the LOR normalization factors. An optimum approach to normalization, especially for 3D PET, remains to be devised.

3.5.4 Scatter Correction

Like randoms, scatter results in generally diffuse background counts in reconstructed PET images, reducing contrast and distorting the relationship between image intensity and activity concentration. Scatter is particularly problematic in PET because of the wide energy windows, about 250 to 600 keV used to maintain high sensitivity in the face of the relatively coarse energy resolution (10% or greater) of PET detectors. In 2D PET, scatter correction is rather straightforward. Once the randoms correction has been applied, the peripheral “tails” in the projection image count profiles, presumably due exclusively to scatter, are fit to a mathematical function and then subtracted (deconvolved) from the measured profile to yield scatter corrected profiles for tomographic image reconstruction. Although this approach works reasonably well for 2D PET and small source volumes (e.g., the brain) in 3D PET, it is not adequate for 3D PET generally. Scatter corrections for 3D PET include: dual energy window based approaches; convolution/deconvolution-based approaches (analogous to the correction in 2D PET); direct estimation of scatter distribution (by Monte Carlo
simulation of the imaging system); and iterative reconstruction based scatter compensation approaches (also employing Monte Carlo simulation). The Monte Carlo simulation and subtraction of scatter are now practical and have been implemented in commercial PET scanners.

### 3.5.5 Attenuation Correction

Attenuation correction is the largest correction in PET. However, one of the most attractive features of PET is the relative ease of applying accurate and precise corrections for attenuation, based on the fact that attenuation depends only on the total thickness of the attenuation medium (Fig. 17). For a positron emitting source and a volume of thickness $L$, the attenuation factor is $e^{-L}$ and the attenuation correction factor $e^{-L}$ regardless of the position of the source. Accordingly, a rod source of a positron emitter such as germanium-68 may be extended along the axial FOV and rotated around the periphery of the FOV first with and then without the patient in the imaging position to acquire the transmission and blank scans, respectively. The *attenuation correction factor* (ACF) can then be derived from the ratio of the counts in these respective scans:

$$AFC_{ij} = e^{-L_{ij}} = \frac{[C]_{Blank}_{ij}}{[C]_{Trans}_{ij}} \quad (3.6.5-1)$$

where $AFC_{ij}$ the attenuation correction factor between coincident detectors $i$ and $j$, $L_{ij}$ is the thickness of the volume between coincident detectors $i$ and $j$, and $[C]_{Blank}_{ij}$ and $[C]_{Trans}_{ij}$, the external source counts between detectors $i$ and $j$ in the blank and transmission scans, respectively. In practice, a blank scan is acquired only once a day. The transmission scan can be acquired before the patient has been injected with the radiopharmaceutical, after the patient has been injected with the radiopharmaceutical but before or after the emission scan, or after the patient has been injected with the radiopharmaceutical.
and at the same time as the emission scan. Preinjection transmission scanning avoids any interferences between the emission and transmission data but requires that the patient remain on the imaging table before, during, and after injection of the radiotracer. It is the least efficient operationally and is rarely used in practice. Postinjection transmission scanning minimizes the effects of patient motion, relying on the much higher external-source count rates for reliable subtraction of the emission counts from the transmission counts. It is probably the most commonly used approach in “PET-only” scanners. Simultaneous emission/transmission scanning is obviously the most efficient (fastest) approach but may result in excessively high randoms and scatter counter rates in the emission data.

A notable refinement of transmission scan-based attenuation correction is the use of a single-photon emitter such as cesium-137 in place of a positron emitter. For equal activity sources, germanium-68 results in much lower count rates and longer transmission scan times than cesium-137 because coincidence counting of the germanium-68 results in rejection of most of its annihilation -rays. In addition, cesium-137 (30 years) has a much longer half-life than germanium-68 (287 days), and therefore a cesium-137 transmission source does not have to be replaced while a germanium-68 source must be replaced periodically. At the same time, the energy of the cesium-137 γ-ray, 662 keV, is significantly higher than that of the 511-keV annihilation γ-rays and, with the excellent energy resolution of GSO, there is less interference of a cesium-137 transmission scan by activity in the patient. As a result, transmission scans can be acquired more quickly since the counting statistics requirements are considerably less than for reliable subtraction of equal energy transmission and emission counts. However, because of the difference in energies, 662 versus 511 keV, the ACFs derived from a cesium-137 transmission scan must be scaled slightly to adjust for the differential attenuation between 662- and 511-keV γ-photons.

Another important advance in transmission scan-based attenuation correction is the use of segmentation. In segmented attenuation correction, the regional ACFs are not measured. Rather, the transmission scan is used to visualize the patient’s internal anatomy and then partition, or segment, it into the visualizable compartments of soft tissue, bone, and lung (air). The appropriate linear attenuation coefficients (μ) - for 511 keV γ-rays, 0.095 cm for soft tissue, 0.13 cm for bone, and 0.035 cm for lung - are then applied to these respective tissue compartments and the overall ACFs calculated. An important advantage of this approach is that far fewer counts are required in the transmission data. As a result, transmission scans for segmented attenuation correction are much faster, only 1 to 2 min, than for nonsegmented correction (4 to 6 min). With the introduction of PET-CT scanners, attenuation correction may now be performed using CT rather than transmission sources. A CT image is basically a two-dimensional map of attenuation coefficients at the CT x-ray energy (80 keV). For attenuation correction of the PET emission data, however, these must be appropriately scaled to the 511 keV energy of the annihilation γ rays. The mass-attenuation coefficients (cm²/gr) for CT x-rays (80 keV) and for 511 keV annihilation γ rays are 0.182 and 0.096 cm² /gr, 0.209 and 0.093 cm² /gm, and 0.167 and 0.087 cm² /gm in soft tissue, bone, and lung, respectively. The corresponding m ratios are therefore 1.90, 2.26, and 1.92, respectively. Thus, ACFs derived from CT images cannot be scaled to those for 511 keV annihilation γ rays simply using a global factor. Accordingly, CT-based attenuation correction in PET has been implemented using a combination of segmentation, to delineate the soft tissue, bone, and lung compartment and variable scaling, to account for the different m ratios in these respective tissues. Commercial PET-CT scanners employ high-end (up to 16 slices) spiral CT scanners, and CT-based attenuation correction therefore not only provides optimal segmentation of tissue compartments but is also much faster than transmission-based corrections. However, CT based attenuation correction is not without complications. Most notably, in areas of the body with materials (such as metallic implants or foci of intravenous contrast) with radiodensities far higher than those for tissues, the attenuation may be over-corrected, resulting in the calculation of spuriously high activity concentrations.
3.5.6 Introduction in PET-CT

Basically a PET – CT scanner is consisted by three major parts:

1. A PET scanner
2. A CT scanner
3. A bed

Currently, on all the commercial systems each module has its own independent detectors, electronics and acquisition system. In a typical system a single bed moves axially into the scanner while the patient receives first a CT scan and then a PET. Even though many of the design challenges in the scanner, such as the gantry rotation and data collection, have already been solved in their independent scanner technologies, the combination of the two systems still presents several challenges. For instance, the patient bed needed to redesigned to reduce vertical deflection as it is traveled into the axial field of view. Because the original beds would have resulted serious misalignment between the scans.

Many PET-CT scanners have a port with larger diameter than the stand-alone PET scanners. Usually a CT scanner has a port with diameter of 70cm, whereas a PET scanner has a port diameter of 60cm. Moderns PET-CT scanner have a port diameter of 70cm to match the CT port facilitating the scanning of overweighted patients and enabling the use of CT protocols which require the positioning of the patient's arms above the head. This wider port required the reduction of the detector module and shielding. Another change at the common PET scanner is the use of a smaller detector ring diameter to reduce external dimensions. During fully 3D PET acquisition, the combined effect of the reduced end shielding and reduced detector ring diameter leads to wider field of view for random and scattered coincidences. Even with accurate scatter and random coincidences correction, the increased level of these factors lead to in increased noise in the final image.

In a typical PET-CT examination, the operator initiates a whole-body scout CT scan (~2-20 sec), to select a scan region. Then a whole-body helical CT scan (~30 sec -2 min) precedes the PET scan (~5 -45min). After CT acquisition a computer corrects and reconstructs the Houshfield data to an image display. Then in order to perform the CT based attenuation correction the original image is down sampled to PET resolution and translated (scaled with bilinear or hybrid method) to 511keV. The translated image is forward projected into PET data format and used to correct the original PET emission data. The reconstruction of the PET image is done. Finally, the two images are overlaid and displayed on the shared console.

The combination of anatomical and functional information in one image is called fusion. It should be noted that the images are not fused in one and there in no DICOM mechanism for travelling fused PET-CT images. The term fusion is used as the display of two distinct images on the same display and it is better denoted as merged. There are several methods for fusing images in one display, commonly is used the alpha blending. In this method the pixel values in the PET image are averaged over those of the CT image. The contribution of the PET versus the CT varies according the $\alpha$ term, which ranges from 0 -> 1. Sometimes the side by side viewing of CT and PET images with locked cursors because the overlying images causes reduction on the resolution of the CT images.

Although the registration algorithms are very advanced alignment error often occur because of patient movement and respiration or cardiac motion. The accurate alignment of the two gantries is very important. No standards for testing the alignment currently exists.

The CT rapidly captures images so the respiration movement does affect the final images. But the PET images which require much longer time, capture an averaged respiratory cycle. Several organ amongst them the liver and spleen experience deviations both in volume and position during respiration. Statistically across many cases, these organs deviations between the scans are modest, but in individual cases these deviations could result inaccurate localization. Choosing an optimal breathing...
protocol could minimize these deviations.

### 3.5.7 Image Reconstruction

Formation of quantitative PET images requires the following data sets: an emission data file to be reconstructed; a normalization file for correction of the emission data for system response; a CT or a transmission data file for attenuation correction; and a corresponding blank (or “air”) file for attenuation correction. In 2D PET, the emission data are the one-dimensional projections (sets of parallel line-integrals) of the direct planes at the azimuthal, or projection, angles relative to the axis of the scanner. The full set of 2D projection data are usually represented as a two-dimensional matrix in polar coordinates (distance $x_r$, angle $\theta$) known as a “sinogram” (or “histogram”) in which each row represents the projected intensity across a single direct plane and each column the projected intensity at the same distance $x_r$ across the projection at successive azimuthal angles. In 3D PET, the projections are two-dimensional $(x_r,y_r)$ parallel line-integrals with azimuthal angle and oblique, or polar, angle. The full set of 3D projection data are then represented as a set of sinograms, with one sinogram per polar angle. In each sinogram, each row represents the projected intensity across a single oblique plane (at polar angle) and each column the projected intensity at the same position across the projection at successive azimuthal angles. Analytic methods for reconstruction of 3D data characteristically suffer from incomplete sampling of the 3D volume as a result of the finite axial FOV of PET scanners.

The 3D re-projection (3DRP) algorithm, an extension of the standard 2D FBP algorithm (see below), has been the most widely used 3D reconstruction algorithm and has been implemented on commercial 3D scanners. In 3DRP, unsampled data are estimated by reconstruction and then 3D forward-projection of an initial image set obtained by reconstruction of the directly measured data. Such 3D reconstruction algorithms remain computer-intensive and rather slow by clinical standards, however. In addition, 3D PET emission data files are very large. If $N_T$ is the total size (in bytes) of the projection data set, $N_R$ is the number of detector rings $\sim 24$ (typical value), $N_d$ the number of detector elements per ring $\sim 512$ (typical value), and $N_b$ the depth of the data storage bins $= 2$ bytes

$$N_T = N_R \frac{N_d}{2} N_d = 0.3 \text{ MByte} \quad (3.6.6-1)$$

for 2D PET and

$$N_T = N_R^2 \frac{N_d^2}{2} N_b = 75 \text{ MBytes} \quad (3.6.6-2)$$

of 3D PET. Thus 3D data sets are more than two orders of magnitude larger than 2D data sets. It is preferable, therefore, to reduce 3D data sets to a more manageable size for image reconstruction, by re-binning of the 3D set of oblique sinograms into a smaller number of direct 2D sinograms. The simplest method is “single-slice re-binning (SSRB)” wherein true oblique LORs are assigned to the direct plane midway between the two detector elements actually in coincidence. Although still used on Anger camera-based systems, SSRB distorts off-axis activity and thus is accurate only for activity distributions close to the detector axis, as in brain or small-animal imaging. A second method is multi-slice re-binning (MSRB), which is fast but is susceptible to “noise” related artifacts. The current method of choice is Fourier re-binning (FORE), based on the 2D Fourier transform of the oblique sinograms. In contrast to SSRB and MSRB, however, FORE cannot be performed in real-time and thus requires the full 3D data set.

After 2D re-binning of 3D data, 2D reconstruction algorithms can used for 3D as well as 2D
PET data. Note that processing of the emission data after the real-time deadtime and random corrections and before image reconstruction - namely, normalization, scatter correction, and then attenuation correction - is normally performed in sinogram space.

One of the most widely used algorithms for reconstruction of tomographic images from 2D data (or 3D data re-binned into 2D projections) - in SPECT as well as PET - remains filtered backprojection (FBP). The basic procedure is as follows: each projection is Fourier transformed from real to frequency space; the projection is filtered in frequency space using a ramp filter; the filtered projection is inverse Fourier transformed from frequency back to real space; and the filtered projection data in real space are uniformly distributed, or back-projected, over the reconstructed image matrix. The resulting reconstructed image is inexact, however, because the ramp filter results in the inclusion of spatial frequencies beyond the maximum frequency image-able by the scanner (ie, the Nyquist frequency, *N*) - producing aliasing artifacts (such as the “starburst” pattern emanating from discrete, high-activity foci) - and amplifies statistical uncertainty (noise or mottle). To compensate for these effects, low-pass, or apodizing, filters (known as Hanning, Butterworth, etc.) are used in place of the ramp filter to eliminate those spatial frequencies above a cut-off frequency, *c*, set equal to *N* or some fraction thereof. Although the resulting reconstructed images have somewhat degraded spatial resolution, they are far less “noisy” (mottled). In contrast to so-called “transform” reconstruction methods such as FBP, iterative algorithms attempt to progressively refine estimates of the activity distribution, rather than directly calculate the distribution, by maximizing or minimizing some “target function”. The solution is said to “converge” when the difference of the target function between successive estimates (iterations) of the activity distribution is less than some prespecified value. Importantly, iterative reconstruction algorithms allow incorporation of realistic modeling of the data acquisition process (including effects of attenuation and of scatter), modeling of statistical noise, and inclusion of pertinent a priori information (eg, only nonnegative count values). The Maximum Likelihood Expectation Maximization (MLEM) algorithm is based on maximizing the logarithm of a Poisson-likelihood target function. The MLEM algorithm suppresses statistical noise, but large numbers of iterations typically are required for convergence and therefore processing times are long. To accelerate this slow convergence, the ordered-subset expectation maximization (OSEM) algorithm groups the projection data into subsets comprised of projections uniformly distributed around the source volume. The OSEM algorithm, which is a modified version of the MLEM algorithm in that the target is still maximization of the log-likelihood function, converges more rapidly than MLEM and is now the most widely used iterative reconstruction method in PET as well as SPECT. The row-action maximization-likelihood (RAMLA) algorithm, related to the OSEM algorithm, has been implemented for direct reconstruction of 3D PET data in the C-PET and Allegro (Philips ADAC). The so-called 3D-RAMLA algorithm, which eliminates 2D re-binning of the 3D data, employs partially overlapping, spherically symmetric volume elements called “blobs” in place of voxels. Reconstruction times are fairly long by clinical standards but the results have been excellent.

### 3.5.8 Quantization

Once the PET emission data have been corrected for deadtime, randoms, system response (by normalization), scatter, and attenuation, the count rate per voxel in the reconstructed tomographic images is proportional to the local activity concentration. To make the images quantitative, then, the count rate per voxel (cps), *C*<sub>ijk</sub>, in voxel *ijk* should be divided by the measured system calibration factor ([cps/voxel]/[μCi/cc]), CF, to yield the activity concentration:

\[ A_{ijk} = \frac{C_{ijk}}{CF} \]  

(3.6.7-1)
where \([A]_{ijk}\) the activity concentration \((\mu Ci/cc)\) in voxel \(ijk\). The calibration factor \(CF\) can be derived by scanning a calibrated standard, that is, a water-filled or water (tissue)-equivalent volume source with all linear dimensions at least twice that of the system spatial resolution (FWHM) and with a uniform, well-defined activity concentration at the time of the scan. The requirement for water equivalence is to ensure that effects such as scatter and attenuation are comparable in both the patient and the standard. And the requirement for linear dimensions at least twice that of the system spatial resolution is to ensure that the effect of partial volume averaging and associated underestimation of local count rates are negligible. (Unless corrected for partial-volume averaging based on some independent measure of size, activity concentrations cannot be reliably determined in structures with dimensions less than twice the system spatial resolution) In principle, assuming the emission data for the patient and the standard are processed identically, the geometry of the standard should be unimportant. In practice, a fairly large source such as cylinder spanning the scanner’s axial FOV and approaching the transverse dimensions of typical patients is preferable. Further, implicit in equation (7) is the assumption that the branching ratios, \(\zeta\), of the positron-emitter administered to the patient and added to the standard are identical. If not, equation (10) must be appropriately adjusted:

\[
[A]_{ijk} = \frac{C_{ijk} \zeta_{\text{Standard}}}{CF \zeta_{\text{Patient}}} \tag{3.6.7-2}
\]

where Patient and Standard the branching ratio of the positron-emitting isotope administered to the patient and added to the standard, respectively. Typically, a more clinically relevant expression of local activity concentration is in terms of the decay-corrected fraction or percent of the administered activity per cubic centimeter (cc). This requires, however, that one precisely assay and record the actual activity in the radiopharmaceutical syringe before and after the injection and record the precise times of the assays and of the scan. The percent of the injected activity per cubic centimeter of tissue, \(\% \text{ ID/cc}\), can then be calculated as follows:

\[
\text{ID/cc} = \frac{C_{ijk} \zeta_{\text{Standard}}}{CF \zeta_{\text{Patient}}} e^{\lambda(t_{\text{scan}} - t_{\text{inj}})} \times 100 \tag{3.6.7-3}
\]

where \(t_{\text{scan}}\) and \(t_{\text{scan}}\) the times of the PET scan and of the radiopharmaceutical injection, respectively, and \((A_{\text{syringe}})_{\text{Pre}}\) and \((A_{\text{syringe}})_{\text{Post}}\) the net activities (decay-corrected to the time of injection) in the radiopharmaceutical syringe before and after the injection, respectively. Clinically, however, the most widely used expression of the activity concentration is the standard uptake value (SUV), the ratio of the activity concentration in tumor or other tissue at the time of the PET scan to that of the mean activity concentration in the total body at the time of injection.
Chapter's References

[4]. PET/CT scanner instrumentation, challenges, and solutions, Adam M. Alessio, PhD, Paul E. Kinahan, PhD, Phillip M. Cheng, MD, Hubert Vesselle, MD, PhD, Joel S. Karp, PhD, Radiol Clin N Am 42 (2004) 1017 – 1032.
4 System Overview

4.1 General Introduction

The planar, small animal, PET system used in the present study was developed by the Detector and Imaging Group, of the Thomas Jefferson National Accelerator Facility in collaboration with the Medical Instruments Technology dep. of the TEI of Athens, the Medical Physics dep. of univ. of Patras and is currently under evaluation in the Institute of Radioisotopes-Radiodiagnostic Products. On Fig.18 is displayed the system's flow diagram.

Figure 18: Systems flow diagram

Table 4.1-1: Photographs displaying various parts of the system (see text).

<table>
<thead>
<tr>
<th>A</th>
<th>B</th>
<th>C</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1.png" alt="Photograph A" /></td>
<td><img src="image2.png" alt="Photograph B" /></td>
<td><img src="image3.png" alt="Photograph C" /></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>D</th>
<th>E</th>
<th>F</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image4.png" alt="Photograph D" /></td>
<td><img src="image5.png" alt="Photograph E" /></td>
<td><img src="image6.png" alt="Photograph F" /></td>
</tr>
</tbody>
</table>
The system is assembled from two detection heads Fig.17.A-F containing two 20x20 pixels LSO crystals with dimensions of 5x5x1 cm³ in order to cover the entire FOV of the two *Hamamatsu H8500* PSPMTs, on which they are coupled (Fig. 17B). Each head includes one PSPMT, one crystal and the read out and pre amplification electronics.

In Fig.17.C is displayed the box that is responsible for the production of the coincidence trigger. Alternative to the trigger box can be used the NIM modules (Fig.17.D). These include the signal discriminator, the gate generator and the coincidence detection (Fig.17.D). The Fig.17.E displays the input plug from the trigger modules and the power supply of the FPGA box.

The anode on the PSPMTs, have 64 (8x8) pads. In order to keep the cost of the read out electronics low, were acquired from 16 channels, which were pre amplified inside the head’s tube. The 8X and 8Y signals were produced as described previously. In addition, due to slight variations in the gain of each pad, leading to distortions in the image, additional resistors were used. These resistors connect each anode pad to the ground. So the gain at each pad is equalized to a universal minimum gain for the whole anode.

After full amplification, the signal (16 channels from each head) is driven to a *data acquisition (DAQ)* system assembled from two DAQ units. Each DAQ unit consists of 16-channel DAQ modules installed on a carrier board with a *high-speed USB 2* interface. Each channel has an independent acquisition unit consisting of traditional *ADC*, *FPGA analog control*, and *FPGA digital processing*. After sampling and processing, the data from each channel are assembled into event blocks for readout by the carrier board. Each event is tagged with a 10 *nsec* time stamp. The time stamp is used to reassemble events distributed across several DAQ units. It can also be used for dynamic studies.

### 4.2 LSO Scintillating crystal

Scintillation detectors are the most common and successful way for detection of 511 keV $\gamma$ photons in PET imaging due to their good stopping efficiency and energy resolution. The LSO crystal is considered to be one of the best choices for the PET systems. The characteristics of these crystal allow very good timing resolution because of the fast scintillating time and the short decay. Thus very accurate *randoms* correction can be achieved. The $Z_{eff}$, the density and the crystal's energy resolution have values that allows the crystal to detect and distinguish efficiently the majority of the emitted $\gamma$ photons in a wide energy range.

### 4.3 Hamamatsu H8500 Flat Panel PSPMT

The PSPMTs we used in this project were the *Hamamatsu H8500*, flat panel multianode PSPMT (Fig.18.A-C). These PSPMTs are optimally designed for small animal imaging, dedicated compact $\gamma$-cameras, scinti-mammography and 2D radiation monitor. They are 52 mm², having a bialkali photocathode and 12 amplification dynodes. The anode has 8 x 8 pixels and its main characteristics are the small dead space and the fast response time, something very useful in conjunction with the very fast LSO crystal. Full specifications are displayed in Table 4.1-1.

#### 4.3.1 Window Material

The borosilicate glass is the most commonly used window material. Because it has a thermal expansion coefficient very close to that of the Kovar alloy which is used for the leads of photomultiplier tubes, it is often called ”Kovar glass”. The borosilicate glass does not transmit ultraviolet radiation shorter than 300 nm. Thus, it is not suited for ultraviolet detection shorter than this wavelength. Moreover, some types of head-on photomultiplier tubes using a bialkali photocathode employ a special borosilicate glass (so-called ”K-free glass”) containing a very small amount of
potassium (K40) which may cause unwanted background counts. The K-free glass is mainly used for photomultiplier tubes designed for scintillation counting where low background counts are desirable.

![Photographs of the PSPMT accompanied with the read out and pre amplification electronics, packed to fit inside the detector head. C. Photograph of the H8550 and H8500B PSPMT, obtained from Hamamatsu data sheets.]

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Description / Value</th>
<th>Unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spectral response</td>
<td>300 to 650</td>
<td>nm</td>
</tr>
<tr>
<td>Peak wavelength</td>
<td>420</td>
<td>nm</td>
</tr>
<tr>
<td>Photocathode material</td>
<td>Bialkali</td>
<td>-</td>
</tr>
<tr>
<td>Window</td>
<td>Material</td>
<td>Borosilicate glass</td>
</tr>
<tr>
<td></td>
<td>Thickness</td>
<td>1.5 mm</td>
</tr>
<tr>
<td>Dynode</td>
<td>Structure</td>
<td>Metal channel dynode</td>
</tr>
<tr>
<td></td>
<td>Number of stages</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>Number of anode pixels</td>
<td>64 (8x8 matrix)</td>
</tr>
<tr>
<td></td>
<td>Pixel size / Pitch at Center</td>
<td>5.8 x 5.8 / 6.08 mm</td>
</tr>
<tr>
<td></td>
<td>Effective area</td>
<td>49 x 49 mm</td>
</tr>
<tr>
<td></td>
<td>Dimensional outline (W x H x D)</td>
<td>52 x 52 x 28 mm</td>
</tr>
<tr>
<td></td>
<td>Packing density (effective area / external size)</td>
<td>89 %</td>
</tr>
<tr>
<td></td>
<td>Weight</td>
<td>140 gr</td>
</tr>
</tbody>
</table>

4.3.2 Cathode material

Since two kinds of alkali metals are employed, these photocathodes are called "bialkali" (Sb-Rb-Cs, Sb-K-Cs). The transmission type of these photocathodes has a spectral response range similar to the Sb-Cs photocathode, but has higher sensitivity and lower dark current. It also provides sensitivity that matches the emission of a NaI:Tl scintillator, thus being widely used for scintillation counting in radiation measurements. On the other hand, the reflection type bialkali photocathodes are fabricated by using the same materials, but different processing. As a result, they offer enhanced sensitivity on the long wavelength side, achieving a spectral response from the ultraviolet region to around 700 nm.

4.3.3 Metal channel dynode

This dynode structure consists of extremely thin electrodes fabricated by Hamamatsu advanced
micromachining technology and precisely stacked according to computer simulation of electron trajectories. Since each dynode is in close proximity to one another, the electron path length is very short ensuring excellent time characteristics and stable gain even in magnetic fields.

### 4.3.4 Flat panel type Multianode PMTs

Metal channel dynodes are mainly used in 1-inch square metal package photomultiplier tubes and flat panel type (2 inch²) photomultiplier tubes, which can be selected according to the particular application. This section introduces a flat panel type photomultiplier tube with an overall height as short as 15 mm. As shown in Fig.19, this photomultiplier tube features a large effective area and minimal dead area (insensitive area).

![Figure 19: History of PMTs.](image)

### 4.3.5 PSPMT Read Out Electronics

The circuit that was used is a resistive matrix built of equal resistors, Table 4.3.5-1. Each pad is connected to two resistors. Since the circuit is symmetrical, it provides anode current division into two equal parts; the first one is flowing into the X output line, and the other one to the Y output line. The X and Y line outputs are connected to the low input impedance current collecting amplifiers. The input characteristics of the amplifiers coupled to the readout matrix outputs, determine the amount of parasitic cross-talk, noise, and circuit operation bandwidth. Table 4.3.5-1.A shows two alternative amplifier circuitry solutions were considered during the development of amplifiers for efficient signal collection with resistive matrix. The first one is a current sensitive amplifier with resistor in feedback while the other one is “a charge sensitive amplifier”, which is an amplifier with capacitor in feedback.

The Table 4.3.5-1.A amplifier circuit has an active input impedance that changes at higher frequencies according to the amplifier gain function. This circuit provides a good crosstalk protection starting from DC which reduces significantly at frequencies over 1 MHz. The Table 4.3.5-1.B amplifier circuit does not show an active input impedance, and which though mostly capacitive. It results a high crosstalk over the input circuit at relative low frequency, but according to the input impedance reduction versus frequency, its crosstalk attenuation increases at higher frequencies and may be even better then for the circuit [A]. In our tests both circuits show a good performance with the readout matrix. However, the circuit [A] has the advantage for fast system design while the circuit [B] is good for large size detectors, where PCB and pad to pad parasitic capacitance crosstalk could dominate over resistive...
4.4 Coincidence Detection: NIM Modules

4.4.1 LeCroy 623B Octal, 100MHz Discriminator

Basic Characteristics:
- NIM packaging
- High speed
- Variable threshold and output width per channel
- Good stability
- No multiple pulsing

4.4.1.1 Generation of Logic Pulses from Analog Signals

A discriminator generates precise logic pulses in response to its input exceeding a given threshold. Output pulses are of standard amplitude and of preset duration or proportional to the input rate. The threshold is a specific voltage of interest to the user (which can be set above some critical noise level or correspond to a physical quantity such as energy). In other applications, the threshold level can correspond to a certain level of integrated rates (coincidence events). The output of a discriminator can be used to trigger or gate associated portions of the data collection system or to generate pulses which are to be counted. It may also be integrated into a complex logic system allowing sophisticated decisions to be made in real time.

LeCroy's family of NIM discriminators offers flexibility and versatility with features such as at least three outputs per channel, adjustable output width and variable threshold level settings. The low minimum threshold levels permit the use of lower gain photomultipliers, long input cables and often avoid the need for preamplifiers.
In this part takes place the set of the H/W thresholds. These thresholds are set by using a capillary or spot source located at the edge of the FOV. The aim is to lower the threshold down to the point that pulses low enough to image the source are accepted. If the thresholds go very low then scattered low energy photons will be accepted, something that will increase the noise and fuzziness.

4.4.1.2 Functional Description

LeCroy's NIM discriminators offer versatility, high speed, multiple input and high performance packaged in single-width NIM modules. All models have small double pulse resolution times and have updating capabilities to reduce dead time. Input signal threshold levels as well as output pulse widths are fully adjustable over a wide range for each channel. Each module offers at least three outputs per channel for added convenience and has a maximum counting rate exceeding 100 MHz. In addition, a common Veto or Inhibit is provided.

Each module offers a variable threshold from -30 mV (-15 mV for the Model 4608C) to -1 V via a front-panel screwdriver adjustment for each channel. The low threshold level is useful when working with signals directly from photomultipliers and other detectors. A monitor point is provided to permit measurement of the threshold level with a voltmeter, assuring accurate results even in varied operating environments. Threshold stability is 0.3%/°C or better. Low input reflections make these units less sensitive to multiple pulsing.

The Model 623B and the Model 821 operate at maximum rates of 100 MHz while the Model 4608C operates up to 150 MHz. All modules have updating capability which permits retriggering while an output from a previous input is still present. A second pulse, which exceeds threshold while an output is already occurring extends the present output by the preset width. However, if the second threshold crossing occurs within the double pulse resolution time, the module will not respond. This configuration is useful when the discriminators are used in DC coincidence logic.

The 821 and 4608C have a selectable Burst Guard operation. In this mode, the output is extended until the falling edge of the last pulse of the burst when input pulses are separated by less than the resolving time. This feature is particularly important when the module is used in Veto applications.

Although the actual width depends on the rate of input and the mode of operation, outputs of the modules are NIM Standard (see Application Note AN-34) level signals with minimum widths set by the front-panel controls. There are a minimum of three standard negative NIM outputs per channel. In addition, the 821 and the 4608C both have one complementary output per channel.

The 4608C includes a built-in test feature which simulates an input signal for each channel. The test feature is enabled with the receipt of a NIM level applied to the front-panel Lemo connector and permits rapid simultaneous testing of all channels.

4.4.2 Ortec 416A Delay and Gate Generator

The generator accepts either polarity of input logic pulse, provides a delay of up to 110 μs, and furnishes an output logic pulse with selected amplitude, polarity, and width. The combination of functions provided by this module satisfies various logic requirements, such as gating multichannel analyzers and alignment of coincidence timing between two channels using dissimilar pulse-shaping modes. Auxiliary outputs include a Delay Period output, with a width equal to the delay time, and a NIM-Standard Fast-negative Delayed Marker pulse. Excellent time stability allows application in systems that require nanosecond time precision. Instruments producing either positive or negative NIM-standard logic signals may be used to drive the Model 416A. Because of the versatility of its amplitude and width adjustments and its dual polarity output connections, the output can be set for compatibility with essentially all nuclear instrumentation. It can also be used as a logical interface between ORTEC equipment and any other instruments.
4.4.3 Ortec 414A Fast Coincidence detection

The ORTEC Model 414A Fast Coincidence is a modular threefold coincidence unit that allows fast coincidence determination between any two or three input signals. The term "fast" indicates the general nature of the coincidence circuit; that is, input pulses are reshaped, and the actual coincidence determination is made on the leading edge, or leading portion, of the pulses. A DC coupled anticoincidence input is provided to inhibit the coincidence output by a DC voltage or a pulse that overlaps the period of coincidence of the coincident pulses. The coincidence inputs are ac-coupled, and all four inputs are controlled by In/Out toggle switches. The resolving time, $2\tau$, of the fast coincidence unit may be varied over a $10$ to $110$ nsec range by a $10$ turn control for accurate resettability of the resolving time. The resolving time of the anticoincidence circuit is set by the width of the input pulse.

Here we can set the appropriate acceptance window. In order to do so, a linear source was imaged and the window was adjusted in order to have a clear and sharp image.

4.5 FPGA electronics

The 32-channel carrier board accepts up to two 16-channel modules. It reads events from the modules and assembles them for readout by the USB host computer. The architecture of the 32-channel unit is shown in Table 4.6-1.A. The carrier provides utilities such as a programmable pulse generator, trigger counters, rate counters, and user-accessible EEPROM. It has two 8 bit powered TTL I/O ports for bidirectional communication with external devices such as level translators, ADCs, DACs, etc. One port is currently configured to input an external TTL trigger and output an integrator gate monitor [1,3].

The system is currently configured to perform simultaneous acquisition on a global trigger. Acquisition is triggered by a TTL signal from the carrier board. The trigger is processed by a non-retriggerable pulse stretcher which then transmitted to all modules simultaneously. After receive confirmation from all modules the carrier instructs the modules to accept events. Otherwise, the income events are cleared. By using trigger handshaking, flexible event buffering, and trigger pulse processing, events can be assembled flawlessly for any trigger rate or pattern.

One channel of the 16-channel DAQ module is shown in Table 4.6-1.B. The analog portion consists of a leading-edge discriminator with 12 bit threshold DAC, an 8 stage 50 nsec delay line, a gated voltage integrator with 12 bit input offset DAC, and a 12 bit 2.5 MHz triggerable SAR ADC. All analog functions are controlled through the FPGA which permits programmable analog control configurations within a channel and between channels. Channel processing may include charge window discrimination, sparsified readout, offset and gain correction, pulse width measurement, histogramming, etc. Event processing may include event assembly, counting, buffering, window discrimination, veto, etc. Utility functions may include programmable trigger pattern, dynamic offset, etc. Events can be tagged with a high-resolution time stamp from a digital counter. While a 10 nsec time stamp is currently used for event assembly, 15ns has been successfully tested and higher resolutions are possible [1,3].

4.6 Kmax Tool sheet

A GUI tool sheet was developed in Kmax, using JAVA, in order to interface between the system and the user. Kmax is multi-parameter, list mode data acquisition and process control environment. Kmax can be used to configure and operate data acquisition and process control systems which use modular instrumentation. Kmax provides high level features for data display and analysis. The Kmax environment can be configured to operate remote hardware via its powerful client / server features.

The tool sheet is separated into 6 tabs (different pages). Each tab is devoted to a different settings group or function. A seventh tab hosts the JAVA methods. In order to communicate the tool sheet with the system we didn't use the standard Kmax routine. Instead a DLL (Direct Linking Library)
was developed which provided all the necessary functions to communicate with the USB interface and translate the functions to methods.

Table 4.6-1: One channel of the 16 channels DAQ module B: Architecture of our 32bit DAQ system.

![Diagram A: Diagram B:](image)

### 4.6.1 Control Panel

The “Control Panel” tab is the main panel used for calibrating the system (Fig.21). In the toolsheet figure, with red letters are denoted the parts to be comment.

A: Pedestal correction. The pedestal correction has to do with the distortions of the ADCs response. Each ADC has a dark current response, in order to cancel this effect on the final image we have to detect on each acquisition channel the bin with the max response and then divide the raw energy signal by this compress factor. In the case this correction is not applied the resulting inhomogeneity of the image is demonstrated in Fig 21 A & B.

B: START / STOP button box. The main control box. The START button starts the acquisition and the STOP stops the procedure. The acquisition may be done using for stop the total time or the final number of counts. This features are very useful is particular type of tests where fix number of counts are needed in order to have reproductivity of the results or the same acquisition time to have to see the evolution of a procedure over fixed time intervals. Furthermore the update time interval may be adjusted.

C: Level Factor: This factor is used to define the the minimum photon energy that will be accepted as true event. The Level factor is compared to the computed sum from all the anode pads.

D: Raw Image Offset, Magnification Factor: Are coefficients which place the COG. The x and y position of COG is calculated by

\[
COG_{xy} = \frac{r_y COG_c \cdot MF}{S_{dim}} + RIO + 0.5 \tag{4.6.1-1}
\]

where \(COG_c\) is the raw COG, \(MF\) is the Magnification Factor, \(S_{dim}\) is the sum of each raw / column,
RIO is the Raw Image Offset. In addition a 0.5 is added in order to round the result. For the calculation of the COGc the following formula is applied

\[ x/y \text{COG}_c = \sum \text{rows/col} \times x/y \text{Pos} \quad (4.6.1-2) \]

where the sum from each row or column is multiplied by the value of each pad.

E: Raw Image A-B: In these two histogram boxes the raw images from the two heads are displayed. The raw images are created by plotting the x and y of all γ photons that are detected on each head, without taking into consideration the existence of coincidence between the two adjacent γ photons. In formula 4.6.1-2 is the x/yPos factor. Under the raw images are located check boxes with which the orientation of the images can be adjusted.

E: Here are displayed the raw energy sums. In other words here are plotted the amplitude of each pulse that surpasses the thresholds (not only the Level Factor but also the H/W threshold). The amplitude is the sum of the values of all the anode pads.

F: Mapped image. Here the raw images are displayed after the LUT (see below) has been applied. The LUT is a table which is used to cluster adjacent points into pixels. The Gaussian spread of the calculated position of detection derives from the stochastic nature of the cameras components. For example the same energy γ-photons don't produce every time the same amount of optical photons, and from this amount of produced photons not every time the same percentage is detected and counted. Furthermore there is a stochastic response of the electronic parts. All these facts lead to a spread on the calculated detection position. The color of each pixels is the sum of all the events in its boundaries, thus the total number of events.

G: Corrected Energy Spectra. These are the spectra after the repositioning of the counts. The γ-photons that are detected at the edges of the FOV appear to have less energy, because part of the produced optical photons are not detected by the PMT. So, depending on the place of the detection a correction has to be applied to recalculate the energy of the pulse. This is the reason why the energy calibration takes place (see below).
Figure 21: Control Panel
4.6.2 Channels

This is a simple tab, which displays the response of each channel. Here we can see if the applied amplification saturates the system. The first 16 channels are from the first PSPMT and the next 16 from the second.

Figure 22: Channels Panel
4.6.3 Look Up Table

In this tab we may insert the appropriate LUT for each head. In order to create the LUT we must extract the raw images from the “Control Panel” tool sheet. And then apply appropriate filters to cluster the count around each hot spot into distinct pixels (Fig.23). Below the LUT we can see the energy LUTs (see energy calibration paragraph).

![LUT Panel]

Figure 23: LUT Panel

4.6.4 Energy Calibration

Here is the place where the energy response of each pixel in examined. As mentioned before, if we put a flood source between the heads the produced image, won't be uniform. The periphery will be depressed. The reason is that some of the produced optical photons, on the periphery will not been detected.

In this procedure we apply a flood source and we take an image with uniform exposure, then we locate the peaks on the response spectrum of every pixel and scale it properly to have the same response on every pixel. The procedure takes some time because a lot of counts have to be accumulated. In Fig.25 we can see a response spectrum, with the peak already marked. In the first scrolled box are plotted all the response spectra from all pixels and below are plotted only the peaks from the the pixel responses.

The shape of the individual spectra depends on the position of the pixel the pixels at the center
of the field of view have a more normal shape, the pixels on the periphery of the FOV have more photon on the low energy bins (Fig 24).

Figure 24: The position of the absorbed photon affects its energy.

Figure 25: Energy Calibration Tab
4.6.5 Reconstruction tab

In the tab which is devoted for the reconstructed image are displayed all options about the production of the final image. First of all we may see a copy of the mapped images and their individual corrected spectra. From these spectra by moving the red cursors we can adjust the area that we want to be used for the construction of the final image. So it is possible to cut all the low energy, scattered γ-photons, that by mistake or false calculation were taken into consideration. Finally we can see the reconstructed images for the middle field and 5, 10, 15 mm away from it (Fig. 26). The different reconstruction fields don’t have to do with real tomography. It comes from the choice of the center plane location option, which is the half of the distance between the two heads.

![Graphical representation of the different reconstruction fields](image)

Options of the reconstruction can be set here. These are the distance between the two heads, the acceptance angle (see chapter about PET physics), the pixel size, the update interval and values about dynamic images.

The distance between the two heads is the distance between the two head tube surfaces.

The pixel size refers to the size in mm of the crystal pixel.

The dynamic imaging works like an oscilloscope. The pixels that receive more γ-counts stay lighted for more time. So the two values that we may adjust are the timing threshold which is the lower time a pixel has to receive counts in order to “light” and the value about the speed which the pixel will fade out.

The distance between the two heads as well as the pixel size are used for the calculation of the ray’s angle. The angle is calculated as show below and is used in order to compare it with the maximum acceptance angle. The effect of the acceptance angle into the final image is well described to the results.
chapter. The systems when is called to compare the angle of the ray with angles above the angle given of this formula fails.

**Figure 27:** Graphical representation of the acceptance angle

**Figure 28:** Reconstruction tab
4.7 USB – Universal Serial Bus

The USB protocol, today, is the most common and efficient way to connect a PC with its peripherals. It was first introduced during 2002 and rapidly involved to the main connection interface. Some of the reasons are the following:

- Easy to use, there is no need to fiddle with configuration and setup details
- Fast, so the interface doesn’t become the communication “bottleneck”
- Reliable, the very few errors are easily detectable
- Versatile, many kinds of peripherals can use this interface
- Inexpensive
- Power conserving

All of these reasons, plus more, led to the choice of the USB interface for our project. Nowadays USB has come to its second version. Which is faster and more reliable. A brief analysis of the USB 2 interface is going to follow, just to introduce the techniques that were used during signal read out for further reading the ...... is recommended.

4.7.1 Topology

The topology, or arrangement of connections, on the bus is a tiered star. At the center of each star is a hub. Each point on a star is a device that connects to a port on a hub. The number of points on each star can vary, with a typical hub having two, four, or seven ports. When there are multiple hubs in series, you can think of them as connecting in a tier, or series, one above the next. The tiered star describes only the physical connections. In programming, all that matters is the logical connection. To communicate, the host and device don’t need to know or care how many hubs the communication passes through. Only one device at a time can communicate with a host controller. To increase the available bandwidth for USB devices, a PC can have multiple host controllers. Some devices are compound devices that contain both a peripheral and a hub. You can cascade up to five external hubs in series, up to a total of 127 peripherals and hubs including the root hub.

However, it may be impractical to have this many devices communicating with a single host controller. In some cases, especially with compound devices where the hubs are hidden inside the peripherals, the peripherals may appear to be using a daisy-chain type of connection, where each new peripheral hooks to the last one in a chain. But the USB’s topology is more flexible and complicated than a daisy chain. Each peripheral connects to a hub that manages communications with the host, and the peripherals and hubs aren’t limited to connecting in a single chain.

4.7.2 Function

The USB specification defines a function as a device that provides a capability to the host. Examples of functions are a mouse, a set of speakers, or a data-acquisition unit. A single physical device can contain before than one function.

4.7.2.1 Hub

A hub has one upstream connector for communicating with the host and one or more downstream connectors or internal connections to embedded devices. Each downstream connector or internal connection represents a USB port.

A 1.x hub repeats received USB traffic in both directions, manages power, and sends and responds to status and control messages. A 2.0 hub does all of this and also supports high speed, converting as needed between speeds.
4.7.3 Device

The USB specification’s definition of a device is a function or a hub, except for the special case of the compound device, which contains a hub and one or more functions. The host treats a compound device in much the same way as if the hub and its functions were separate physical devices. Every device on the bus has a unique address, except again for a compound device, whose hub and functions each have unique addresses.

A composite device is a multi-function device with multiple, independent interfaces. The interfaces are defined by interface descriptors stored in the device. A composite device has one address on the bus but each interface has a different function and specifies its own device driver on the host. For example, a composite device could have one interface for an audio device and another interface for a control panel.

4.7.4 Port

In a general sense, a computer port is an addressable location that is available for attaching additional circuits. Usually the circuits terminate at a connector that enables attaching a cable to a peripheral. Some peripheral circuits are hard-wired to a port. Software can monitor and control the port circuits by reading and writing to the port’s address. Computer memory also consists of addressable locations, but the CPU typically accesses memory with different machine instructions than are used for accessing ports. USB ports differ from many other ports because all of the ports on a bus share a single path to the host and aren’t directly addressable. With the RS-232 interface, each port is on the PC and independent from the others. If you have two RS-232 ports, each has its own data path, and each cable carries its own data and no one else’s. The two ports can send and receive data at the same time. With USB, each host controller manages a single bus, or data path. Each connector on a bus represents a USB port, but unlike RS-232, all devices share the bus’s bandwidth. So even though a USB host controller can communicate with multiple ports, each with its own connector and cable, one data path serves all. Only one device or the host may transmit at a time. A single computer can have multiple USB host controllers, however, each with its own bus. Other interfaces where multiple devices can share a data path include IEEE-1394, SCSI, and Ethernet. Another difference with USB is that a bus can have ports on hubs that are external to the host controller’s PC.

4.7.5 Division of Labor

The host and its devices each have defined responsibilities. The host bears most of the burden of managing communications, but a device must have the intelligence to respond to communications and other bus events from the host and the hub the device attaches to.

The Host’s Duties

To communicate with USB devices, a computer needs hardware and software support that enable the computer to function as a USB host. The hardware consists of a USB host controller and a root hub with one or more USB ports. The software support is an operating system that provides a mechanism for sss/ to communicate with the USB aware. Just about any recent PC will have a USB host controller and two or more USB-port connectors. Many PCs have multiple host controllers. If a computer doesn’t have USB support built into its motherboard, you can add a host controller on an expansion card that plugs into a slot on the PCI bus. For portable computers, USB controllers on PC cards are available. The host is in charge of the bus. The host has to know what devices are on the bus and the capabilities of each device. The host must also do its best to ensure that all devices on the bus can send and receive data as needed. A bus may have many devices, each with different requirements,
and all wanting to transfer data at the same time. The host’s job is not trivial. Fortunately, the host-controller hardware and the host-controller drivers in Windows do much of the work of managing the bus. Each device attached to the host must also have a device driver that enables applications to communicate with the device. Some peripherals can use device drivers included with Windows. Other devices use drivers provided by the device manufacturer. Various system-level software components manage communications between the device driver and the host-controller and root-hub hardware. applications don’t have to worry about the USB-specific details of communicating with devices. All the application has to do is send and receive data using standard operating-system functions that are accessible from just about all programming languages. Often the application doesn’t have to know or care whether the device uses USB or another interface. The host performs the tasks below. The descriptions are in general terms. Later chapters have more specifics.

4.7.6 Detect Devices

On power-up, the hubs make the host aware of all attached USB devices. In a process called enumeration, the host assigns an address and requests additional information from each device. After power-up, whenever a device is removed or attached, the host learns of the event and enumerates any newly attached device and removes any detached device from its list of devices available to applications.

4.7.7 Manage Data Flow

The host manages the flow of data on the bus. Multiple peripherals may want to transfer data at the same time. The host controller divides the available time into segments called frames and microframes and gives each transmission a portion of a frame or microframe. Transfers that must occur at specific rate are guaranteed to have the amount of time they need in each frame. During enumeration, a device’s driver requests the bandwidth it will need for any transfers that must have guaranteed timing. If the bandwidth isn’t available, the host doesn’t allow communications to begin. The driver must then request a smaller portion of the bandwidth or wait until the requested bandwidth is available. Transfers that have no guaranteed timing use the remaining portion of the frames and must wait if the bus is busy.

4.7.8 Error Checking

When transferring data, the host adds error-checking bits. On receiving data, the device performs calculations on the data and compares the results with the received error-checking bits. If the results don’t match, the device doesn’t acknowledge receiving the data and the host knows that it should retransmit. USB also supports one transfer type that doesn’t allow re-transmitting, in the interest of maintaining a constant transfer rate. In a similar way, the host error-checks the data received from devices. The host may receive other indications that a device can’t send or receive data. The host can then inform the device’s driver of the problem, and the driver can notify the application so it can take appropriate action.

4.7.9 Provide Power

In addition to its two signal wires, a USB cable has +5V and ground wires. Some devices draw all of their power from these wires. The host provides power to all devices on power-up or attachment,
and works with the devices to conserve power when possible. A high-power, bus-powered device can
draw up to 500 milliamperes. The ports on a battery-powered host or hub may support only low-power
devices, which are limited to 100 milliamperes. A device may also have its own power supply.
Exchange Data with Peripherals All of the above tasks support the host’s main job, which is to
exchange data with peripherals. In some cases, a device driver requests the host to attempt to send or
receive data at defined intervals, while in others the host communicates only when an application or
other software component requests a transfer. The device driver reports any problems to the appropriate
application.

4.7.10 The Peripheral’s Duties

In many ways, the peripheral’s duties are a mirror image of the host’s. When the host initiates
communications, the peripheral must respond. But peripherals also have duties that are unique. A
peripheral can’t begin USB communications on its own. Instead, the peripheral must wait and respond
to a communication from the host. (An exception is the remote wakeup feature, which enables a
peripheral to request communications from the host.) The USB controller in the peripheral handles
many of the device’s responsibilities in hardware. The amount of support required by device firmware
varies with the chip. The peripheral must perform all of the tasks described below. The descriptions are
in general terms. Later chapters have more specifics.

4.7.11 Detect Communications Directed to the Chip

Each device monitors the device address contained in each communication on the bus. If the
address doesn’t match the device’s stored address, the device ignores the communication. If the address
matches, the device stores the data in its receive buffer and triggers an interrupt to indicate that data has
arrived. In almost all chips, these functions are built into the hardware and require no support in code.
The firmware doesn’t have to take action or make decisions until the chip has detected a
communication containing the device’s address.

4.7.12 Respond to Standard Requests

On power-up, or when the device attaches to a powered system, a device must respond to
standard requests sent by the host during enumeration. The host may also send requests any time after
enumeration completes. All devices must respond to these requests, which query the capabilities and
status of the device or request the device to take other action. On receiving a request, the device places
data or status information in a transmit buffer to send to the host. For some requests, such as selecting a
configuration, the device takes other action in addition to responding with information. The USB
specification defines eleven requests, and a class or vendor may define additional requests. A device
doesn’t have to carry out every request, however; the device just has to respond to the request in an
understandable way. For example, when the host requests a configuration that the device doesn’t
support, the device responds with a code that indicates that the configuration isn’t supported.

4.7.13 Error Check

Like the host, a device adds error-checking bits to the data it sends. On receiving data that
includes error-checking bits, the device does the error-checking calculations. The device’s response or
lack of response tells the host whether to re-transmit. These functions are typically built into the
controller’s hardware and don’t need to be programmed. When appropriate, the device also detects the acknowledgement the host returns on receiving data from the device.

4.7.14 Manage Power

A device may be bus-powered or have its own power supply. For devices that use bus power, when there is no bus activity, the device must limit its use of bus current. When the host enters a low-power state, all communications on the bus cease, including the periodic timing markers the host normally sends. On detecting the absence of bus activity for three milliseconds, a device must enter the Suspend state and limit the current drawn from the bus. While in the Suspend state, the device must continue to monitor the bus and exit the Suspend state when bus activity resumes. Devices that don’t support the remote-wakeup feature should consume no more than 500 microamperes from the bus in the Suspend state. If a device supports the remote-wakeup feature and the host has enabled the feature, the limit is 2.5 milliamperes. These are average values over 1 second; the peak current can be greater.

4.7.15 Exchange Data with the Host

All of the above tasks support the main job of the device’s USB port, which is to exchange data with the host. After being configured, the device must respond to communications that may contain data and may require the device to return data or status information. The device’s capabilities, the host’s device driver, and the applications that use the device together determine the type of communications and when they occur. For most transfers where the host sends data to the device, the device must respond to each transfer attempt by sending a code that indicates whether the device accepted the data or was too busy to handle it. For most transfers where the device sends data to the host, the device must respond to each attempt by returning data or a code indicating there was no data to send or the device was busy. Typically, the hardware responds automatically according to settings made previously in firmware. Some transfers don’t use acknowledgements and the sender assumes the receiver has received all transmitted data. The controller chip’s hardware handles the details of formatting the data for the bus. The formatting includes adding error-checking bits to data to transmit, checking for errors in received data, and sending and receiving the individual bits on the bus. Of course, the device must also do anything else it’s responsible for. For example, a mouse must be ready to detect movement and button clicks, a data-acquisition unit has to read the data from its sensors, and a printer must translate received data into images on paper.

4.7.16 Speed

A device controller may support one or more bus speeds. Virtually all hubs support low- and full-speed devices. The exception is a hub in a compound device whose functions use a single speed. A low- or full-speed peripheral can connect to any USB hub. Users don’t have to know whether a device is low or full speed because there are no user settings or configurations for different speeds. High-speed peripherals are likely to be dual-speed devices that also function at full speed. A 1.x host or hub doesn’t support high speed because high speed didn’t exist when the 1.x specifications were written. To ensure that high-speed devices don’t confuse 1.x hosts and hubs, all high-speed devices must at least respond to standard enumeration requests at full speed. Any host can thus identify any attached device. Other than responding to bus reset and standard requests at full speed, a high-speed device doesn’t have to function at full speed. But because adding support for full speed is easy to do and is required to pass the USB IF’s compliance tests, most high-speed devices also function at full
speed. The actual rate of data transfer between a peripheral and host is less than the bus speed and isn’t always predictable. Some of the transmitted bits are used for identifying, synchronizing, and error-checking, and the data rate also depends on the type of transfer and how busy the bus is.

For time-sensitive data, USB supports transfer types that have a guaranteed rate or guaranteed maximum latency. Isochronous transfers have a guaranteed rate, where the host can request a specific number of bytes to transfer to or from a peripheral at defined intervals. The intervals can be as often as every millisecond at full speed or every 125 microseconds at high speed. Isochronous transfers have no error correcting, however. Interrupt transfers have error correcting and guaranteed maximum latency, which means that a precise rate isn’t guaranteed, but the time between transfer attempts will be no greater than a specified period. At low speed, the requested maximum interval can range from 10 to 255 milliseconds. At full speed, the range is 1 to 255 milliseconds. At high speed, the range is 125 microseconds to 4.096 seconds. Because the bus is shared, there’s no guarantee that a particular rate or maximum latency will be available to a device. If the bus is too busy to allow a requested rate or maximum latency, the host refuses to complete the configuration process that enables the host to attempt the transfers. To take full advantage of reserved bandwidth, the device driver and application software or device firmware must ensure that data is available to send when the host controller is ready to initiate the transfer. The receiver of the data must also be ready to accept the data when it arrives. At full and high speeds, the fastest transfers on an otherwise idle bus are bulk transfers, with a theoretical maximum of 1.216 Megabytes/sec. at full speed and 53.248 Megabytes/sec. at high speed. The host controller may limit a single bulk transfer to a slower rate, however. The transfers with the most guaranteed bandwidth are high-speed interrupt and isochronous transfers at 24.576 Megabytes/second. Although the low-speed bus speed is 1.5 Megabits/sec., the fastest guaranteed delivery for the data in a single transfer is 8 bytes every 10 milliseconds, or just 800 bytes/sec.

4.8 Bitwise Quick USB

After this short introduction in the USB interface follows the description of the Bitwise Quick USB Plug In module which is the one we used. The description comes from the official Quick USB brochure.

The QuickUSB QUSB2 Plug-In Module is a 2” x 1 ½” circuit board that implements a bus-powered Hi-speed USB 2.0 endpoint terminating in a single 80-pin target interface connector.

The target interface consists of:
- One 8 or 16-bit high-speed parallel port
- Up to three general-purpose 8-bit parallel I/O ports
- Two RS-232 ports
- One I2 C port
- One soft SPI port or FPGA configuration port

High-Speed Parallel

The high-speed parallel port is configurable as an 8 or 16 bit synchronous parallel port. It delivers a sustained data rate of up to 12 MB/s and a burst rate of up to 48MB/s. The high-speed interface consists of the data port FD[15:0], control lines CMD_DATA, REN, WEN and GPIFADR [8:0]. The port can be used as a multiplexed command/data bus by decoding CMD_DATA (CMD = 0, DATA = 1 in the target logic. Reads are indicated by REN = 1 and writes are indicated by WEN = 1. If the address bus is configured to be active, concurrent with reads or writes the GPIFADR bus contains the address of each data element read from or written to FD [15:0].
4.8.1 General Purpose Parallel I/O

General purpose I/O pins must be configured to indicate whether they are being used as input or output pins. This is accomplished using library calls documented in the QuickUSB User’s Guide.

The parallel ports have multiple functions and may not be available if alternate functions are enabled. The general-purpose I/O ports are ports A, C & E. Ports B & D are reserved for the High-Speed Parallel port. The Port E alternate function is FPGA configuration and the soft SPI port. If these alternate functions are used, port E is reserved. Otherwise, port E can be used as general-purpose I/O.

4.8.2 RS-232

The module has two RS-232 ports with a configurable baud rate. Both ports use the same baud rate. These interrupt-driven ports internally buffer data as it arrives and when queried return the contents of the internal buffer. The interrupt buffer depth is 32 characters per port.

4.8.3 I2C

An I2C compatible port is included on the QuickUSB module. The port is a bus master only. Address 1 is reserved for on-board functions. The QuickUSB library provides functions to write and read blocks of data to and from I2C peripherals.

4.8.4 SPI

The module supports SPI peripherals through a ‘soft’ SPI port, which uses pins on port E. The pins MOSI, SCK, MISO and nSS are shared with the FPGA configuration function and will not interfere with each other if the SPI peripherals only drive the MISO when nSS is asserted (nSS=0).

4.8.5 FPGA Configuration

The QuickUSB Plug-In module can program SRAM-based Altera programmable logic devices using five pins of port E. When designing your peripheral to use this feature, consult the ‘PS Configuration with a Microprocessor’ section of Altera Application Note 116, ‘Configuring SRAM-Based LUT Devices’. This document specifies the circuitry needed to configure an Altera device with a microcontroller. The QuickUSB module provides the DCLK, DATA0, nCE, nCONFIG, nSTATUS and CONF_DONE signals required to configure Altera devices in passive-serial mode. If more than one Altera device must be configured over the interface, the devices should be ‘daisy-chained’ and the programming files combined into a single ‘RBF’ file. Consult AN116 for details on this configuration or contact Bitwise Systems.

The QuickUSB Library

The QuickUSB™ Library is included with the QUSB2 and provides DLL and C library interfaces to the QuickUSB Plug-in Module. The QuickUSB Library hides the complexity of USB 2.0 behind a port-based programmer’s interface. A complete description of each library function is provided in the QuickUSB™ User’s Guide

4.9 DAQ.DLL

In order to use the Bitwise library which is on C++ and translate it in JAVA which Kmax works
with. A Direct Linking Library was developed. This library contains the jni interface. The Java Native Interface (JNI) is a programming framework that allows Java code running in the Java virtual machine (JVM) to call and be called by native applications (programs specific to a hardware and operating system platform) and libraries written in other languages, such as C, C++ and assembly.

The JNI is used to write native methods to handle situations when an application cannot be written entirely in the Java programming language such as when the standard Java class library does not support the platform-specific features or program library. It is also used to modify an existing application, written in another programming language, to be accessible to Java applications. Many of the standard library classes depend on the JNI to provide functionality to the developer and the user, e.g. I/O file reading and sound capabilities. Including performance- and platform-sensitive API implementations in the standard library allows all Java applications to access this functionality in a safe and platform-independent manner. Before resorting to using the JNI, developers should make sure the functionality is not already provided in the standard libraries.

The JNI framework lets a native method utilize Java objects in the same way that Java code uses these objects. A native method can create Java objects and then inspect and use these objects to perform its tasks. A native method can also inspect and use objects created by Java application code.

JNI is sometimes referred to as the "escape valve" for Java developers because it allows them to add functionality to their Java Application that the Java API can't provide. It can be used to interface with code written in other languages, like C++. It is also used for time-critical calculations or operations like solving complicated mathematical equations, since native code can be faster than JVM code.

4.10 JDAQ.JAR

Here exist all the classes that the tool sheet uses. The Kmax toolsheet is only an interface between the user and the classes that are stored inside this JAR file. The JAR files are convenient libraries used from JAVA.
Chapter's references:
[1]. USB Complete Everything You Need to Develop Custom USB Peripherals, Jan Axelson, Published by Lakeview Research, ISBN13 978-1-931448-03-1
[4]. A novel readout concept for multianode photomultiplier tubes with pad matrix anode layout, Vladimir Popov, Stan Majewski, Benjamin L. Welch.
5 Performance evaluation results

In order to calibrate and evaluate the performance of the system properly, a number of tests were performed, using capillary sources filled with FDG ($^{18}$F). The capillary sources used for this calibration tests had an inner diameter of $1.1 \text{ mm}$. The size of the capillaries does not affect resolution calculations, since the ultimate intrinsic spatial resolution is limited by the size of the crystals and their septa (2mm +0.1 mm).

But the fact that the surrounding material is air leads to worst spacial resolution than the one we would measure if the surrounding material was soft tissue or water. This happens because of the increased range of the β$^+$ particles.

5.1 METHODS

5.1.1 Spatial Resolution

In order to determine the spatial resolution we used the “Full Width at Half Maximum“ FWHM. The FWHM has the size of mm and it is the width of a distribution at the half of its maximum amplitude. The FWHM is the minimum distance which must have two objects in order to be imaged as different structures.

The distribution we used was the “Linear Spread Function”, LSF. In order to extract this distribution from the images of the linear sources, we used the image profiles which were perpendicular to the source, Fig.29. From each one of these profiles we calculated the average profile and used it for the calculation of FWHM.

The spatial resolution was evaluated against the head separation distance, the acceptance angle, and the reconstruction field.

Evaluation tests with more than one sources also took place. These experiments took place with two and three capillary sources. In the case of the two capillary sources was evaluated the effect of the acceptance angle in the distance between the two (or three) capillary sources, Fig.30. The separation distance which was imaged, for two sources, is represented by the following formula

$$x' = x - 2 \times \text{FWHM} \quad (5.1.1-1)$$

where x is the true separation distance and x’ is the imaged separation distance.

Figure 29: Extraction of a random profile and a typical FWHM
5.1.2 Modulation Transfer Function - MTF

MTF is the function that describes the response of the system in different spatial frequencies. In order to calculate it we used the Fourier transformation of mean profile of capillary sources. This is the same profile that was used for the calculation of the FWHM. Before the calculation of MFT a threshold was applied in order to reduce the background noise and so calculate more smoothed MTF curves. Because high frequencies noise would have a negative impact on the MTF curves.

5.1.3 Sensitivity

The sensitivity was evaluated in counts per second per \( mCi \) per \( mm^2 \), \( cps/(mCi*mm^2*sec) \). Using a linear capillary source. The experiments which were used derive from NEMA NU2-2001 and were rescaled for small animal imaging that employs a \(^{18}F\) source. The investigation of the sensitivity took place only for the entire FOV.

In order to evaluate the sensitivity of the system we had to increase the acceptance angle enough to overpass the maximum angle defined of the two diagonals that connect the farthest corners of the two PSPMT. Otherwise a part of the detected events would be rejected (see acceptance angle), Fig.31. In the figure are shown the two detection heads in two different separation distances, assuming that there are only three annihilation events. Then we can see the maximum area that it is possible to be sorted. For particular acceptance angle but bigger head separation distance the sensitivity is better. Because the acceptance areas cover a larger portion of the FOV. But when the acceptance angle cover the entire FOV then the smaller distances have better sensitivity because they are nearer to the source so they detect more \( \gamma \) photons. 

Further more the sensitivity for particular acceptance angle but different separation distances has also been investigated.
5.2 RESULTS

5.2.1 Spatial Resolution

5.2.1.1 Different head separation distances

As we can see from Fig.32, as the separation distance of the two heads takes higher values the FWHM is degraded. This negative impact takes place because of the spread of the $\gamma$-photons. The spatial resolution takes values from $\sim3.38$ mm up to $\sim3.48$ mm, for 40 up to 70 mm separation distance, respectively.

The separation distance that will be used in in vivo experiments will not be bigger than 50 mm. Because it is enough to cycle the mouse without any direct contact.

![Graphical representation of the acceptance angle effect on the sensitivity with respect to the head separation distance](image1)

**Figure 31:** Graphical representation of the acceptance angle effect on the sensitivity with respect to the head separation distance

![Graphical representation of FWHM over Acceptance Angle](image2)

**Figure 32:** FWHM over Acceptance Angle
5.2.1.2 Different acceptance angles

As the acceptance angle takes higher values the distortion in the image leads to decrease the FWHM. This decrease takes place mainly to the center of the field of view which suffers and the greatest distortions. As it is obvious and from the Fig.35 the tube tends to be wider in the center of the FOV. The amount of this distortion is demonstrated in Fig.34 in terms of FWHM. The experiment took place for 3 different distances (40, 70, 100 mm).

![Graph showing FWHM as the acceptance angle takes greater values, for three different acceptance angle](image)

Figure 33: FWHM as the acceptance angle takes greater values, for three different acceptance angle

Initially the FWHM is increased linear until the angle reaches a certain plateau. Afterwards the FWHM is stable. In the 70 and 100 mm separation distances the deviation in the plateau values doesn't allow us to obtain an accurate value for the FWHM. A possible solution would be to increase the acquisition time resulting in increased $\gamma$ photon counts.

The acceptance angle is a very important parameter. If we want to distinguish small details we have to use narrow angle but this will reduce the sensitivity. Reduced sensitivity leads to increase to the acquisition time because otherwise the amount of information would not be enough.
Figure 34: Images obtained by changing the acceptance angle for 40mm separation distance
Figure 35: Images obtained by changing the acceptance angle for 70mm separation distance
Figure 36: Images obtained by changing the acceptance angle for 100mm separation distance
5.2.1.3 Different reconstruction planes

In the reconstruction tab these is the possibility to see the image as if it would be in different locations in the z axis. This movement would result in to degraded spatial resolution. The reason is the wider spread of the rays to one of the two detectors.

In Fig. 38 we can see the FWHM in pixels of the spacial resolution if we move the capillary source from the middle of the distance between the two detectors.

![Figure 37: FWHM in pixels for reconstruction in different planes](image)

5.2.2 Sensitivity

5.2.2.1 Acceptance Angle

As illustrated in Fig. 39, the sensitivity is increased as the acceptance angle takes higher values until it reaches a certain plateau. This plateau is the sensitivity of the camera for the corresponding head separation distance when the acceptance angle doesn't reject any of the detected photons.

For acceptance angles smaller than the one the tangent of the maximum acceptance angle is compared the tangent of the two sides of the triangle which is formed by the imaginary line that connects the surfaces of the two directors, \( \gamma \) ray and the projection of the ray to one of the detectors.

As it has already been described in the Methods section, the sensitivity is better for longer distances because the area of the PSPMT that is covered by the maximum triangle is bigger than for smaller separation distances.
5.2.2.2 Different head separation distances

As is illustrated from the Fig.40, the sensitivity under a particular acceptance angle increases. This takes place because as the head separation distance is increased the base of the triangles, formed by the acceptance angles cover larger area of the detector surface. Therefore a small portion of the total detected events is rejected, Fig.31.

![Figure 38: Sensitivity of the system with respect to the acceptance angle](image)

![Figure 39: Relative sensitivity with respect to the separation distance for constant acceptance angle](image)
5.2.3 Two and Three linear capillary sources

The next performance tests took place with two and three capillaries in four different intercapillary distances and with four different acceptance angles ($3^\circ$, $5^\circ$, $7^\circ$ and $10^\circ$). In these tests the aim was to determine the minimum distance in which two (or three) capillaries are discriminated as separate sources, with respect to the acceptance angle and their distance. The distance between the heads was 75 mm in all measurements. This distance was selected, since it allows acquisition of projection data for tomographic mouse imaging without any direct contact. Results are demonstrated in Figures for two capillary sources and Figure for three capillary sources. As it is shown, when the acceptance angle increases the sources become less discriminated, and tend to be imaged as one source.

[Images showing the results for different separation distances]
5.2.4 In Vivo imaging

In order to assess the performance of the camera in real laboratories imaging two mice where imaged. The subjects were healthy without any malignancies.

The first subject was a living mouse which was imaged 30 min post bolus injection. The
injection had 400μCi FDG. The subject was put to sleep using the following solution: 0.5 ml Ketamin (100mg/ml) - 0.25ml Xylazin (20mg/ml). The acquisition time was 70 sec for each bed position.

Figure 41: The subject that was used for in vivo imaging of living mouse with FDG
Figure 42: Full image of a mouse which was injected with FDG, 50 min prior sacrifice

Figure 43: Normal photograph of the subject
5.2.4.1 Effect of acceptance angle on in vivo images

In the following Fig. 45 we is demonstrated the effect of the acceptance angle in the in vivo images. In the previous chapters we investigated the effect on capillary sources. We concluded in to that as the acceptance angle takes higher values the image is distorted in the center of the FOV by the increased number of events that is being accepted. Thus the edges are depressed. On the other hand that increasing on the acceptance angle leads to better count rate and thus better sensitivity.

Figure 44: Effect of the acceptance angle on in vivo images
Matlab Image Processing Code:

```matlab
% Kmax_Plot_PROC_All ver 0.1
% Creator @ Nikos Efthimiou
% This program is a no interactive saPET data analysis tool. It can operate
% only with horizontal capillary sources. It calculates the FWHM and the
% sensitivity. The difference with the other versions is that this analyses
% the tube at full length.
%------------------------------------------------------------------------
clear all; close all; clc;
[filename,pathname] = uigetfile('*.*','Pick a File','/home/nikos/Documents/Projects/saPET/Results/2008/09/02/MECOLI/RESDIST');
if isequal(filename,0)
    disp('Error on selecting the file');
end
fullpath = sprintf('%s%s',pathname,filename);
fid = fopen(fullfile, 'r');
k=1; l=1;
C = textscan(fid, '%d %d %d %d %d %d %d %d %d %d', 'headerlines', 2, 'CollectOutput', 1);
A=ones(60,60); % for recs
for i=1:1600 % for heads
    for j=1:10
        A(k,l)=C{1,1}(i,j);
        l=l+1;
    end
end
fclose(fid);
final=sprintf('%s%s_c.txt',pathname,filename);
A=imcrop(A,[0 0 40 40]);
A=flipud(A);
k = 0;
save(final,'A','-ASCII');
imagesc(A); figure(gcf); hold on;
B=A;
oo=1;
for i=1:25
    prof=A(:,i);
    flag=0;
    max=0; m=0;
    for j=1:10
        if prof(j)>max
            max=prof(j);
        end
```
m=max; d=0; oneu=0; oned=0; pano_memia=0; kato_memia=0;

if m==0
    FWHM(i)=0;
    continue;
end

prof=prof/m;
aprof(:,:,oo) = prof;
oo=oo+1;
for ii=1:40
    if prof(ii)==0.5 && d==0 && oneu==0
        x11=ii;
        pano_memia=1;
        d=1; oneu=1;
        continue;
    end
    if prof(ii)>0.5 && d==0 && oneu==0
        P11=ii-1;
        P21=ii;
        d=1; oneu=1;
        continue;
    end
    if prof(ii)==0.5 && d==1 && oned==0
        x21=ii;
        kato_memia=1;
        d=0; oned=1;
        continue;
    end
    if prof(ii)<0.5  && d==1 && oned==0
        P31=ii-1;
        P41=ii;
        d=0;oned=1;
        continue;
    end
end

if pano_memia==0
    x11=P11+((0.5-prof(P11))*(P21-P11)/(prof(P21)-prof(P11)));
    if prof(P11)-0.5 > prof(P21) - 0.5
        x11=P21;
    end
    if prof(P11)-0.5 < prof(P21) - 0.5
        x11=P11;
    end
end

if kato_memia==0
    x21=P31+((0.5-prof(P31))*(P41-P31)/(prof(P41)-prof(P31)));
    if prof(P31)-0.5 > prof(P41) - 0.5
        x21=P41;
    end
    if prof(P31)-0.5 < prof(P41) - 0.5
        x21=P31;
    end
end

FWHM(i)=x21-x11;
if FWHM(i)<0
FWHM(i)=0;
end
%clear P11 P21 P31 P41 x11 x21 m profile;
end

ff=mean(FWHM)*1.25; % Auto den isiei giati exoume keno apo stis 2 akres.
iii=0;ff=0;
for i=1:size(FWHM,2);
    if (FWHM(i) ~= 0)
        iii=iii+1;
        ff=FFWHM(i)+ff;
    end
end
ff=(ff/iii)*1.25;
sens=sum(sum(B));
mnn=0;
for i=1:40
    for j=1:40
        if B(i,j)>mnn
            mnn=B(i,j);
        end
    end
end
imagesc(A); figure(gcf);
%   fullpath2 = sprintf('%s%s_profile',pathname,filename);
%  saveas(gcf1,fullpath2,'jpg');

Matlab Image Processing Code 2:

% Creator Nikos Efthimiou
% function Kmax_Plot_Proc
clear all; close all;
[filename,pathname] = uigetfile('*.*', 'Pick a File', '/home/nikos/Documents/Projects/saPET/Results/2008/09/02/MECOLI/RESDIST');
if isequal(filename,0)
    disp('Error on selecting the file');
end
fullpath = sprintf('%s%s_c.txt',pathname,filename);
fid = fopen(fullpath, 'r');
k=1; l=1;
C = textscan(fid, '%d %d %d %d %d %d %d %d %d %d', 'headerlines',2,'CollectOutput',1);
% A=ones(1024,1); % For hists
% A=ones(400,400); % for heads
A=ones(60,60); % for recs
% for i=1:103 %for hists
for i=1:360 %for recs
    % for i=1:16000 % for heads
    for j=1:10
        A(k,l)=C{1,1} (i,j);
        l=l+1;
        if l>60 %for recs
            % if l>400 %for heads
            l=1; k=k+1;
        end
    end
end
fclose(fid);
final=sprintf('%s%s_c.txt',pathname,filename);
A=imcrop(A,[0 0 40 40]);
A=flipud(A);
k = 0; % k = index or ROI selected
save(final,'A','-ASCII');
roi = [];
figure(1); imagesc(A); roipoints = ginput(2);
while isempty(roipoints)==0
    k = k + 1;
    hold on;
    roipoints = round(roipoints);
    if (roipoints(1)==roipoints(2))
        figure(1);
        plot(roipoints(1),0:0.1:41,'r');
        roi{k}=A(:,roipoints(1));
        flag=1;
    end
    if (roipoints(3)==roipoints(4))
        figure(1);
        plot(0:0.1:41,roipoints(3),'r');
        roi{k}=A(roipoints(3),:);
        flag=2;
    end
    max_roi  = max(roi{k});
    roi{k} = roi{k}/max_roi;
    % plot roi as a new small image
    figure(2);
    for kk=1:k
        %hold on;
        subplot(1,3,kk); % 5 in each row
        plot(roi{kk}); title(['ROI ', num2str(kk)]);
        %plot (0:0.1:40,0.5,'r');
    end
    % save roi as an image file
    roiFilename = [final,'_ROI_' num2str(k),'.txt'];
    dummy_roi = roi{k};
    save(roiFilename,'dummy_roi','-ASCII');
    % select next roi
    figure(2); FWHM_p = ginput(2); % ATTENTION! X-coordinate is the image column (which is the 2nd argument in array 'im'), and Y-coordinate is the image row (which is the 1st argument in array 'im')
    if (flag==1)
        FWHM(k)=FWHM_p(2)-FWHM_p(1);
        FWHM(k)=1.25*FWHM(k);
    end
    figure(1); roipoints = ginput(2); % ATTENTION! X-coordinate is the image column (which is the 2nd argument in array 'im'), and Y-coordinate is the image row (which is the 1st argument in array 'im')
end
fFWHM = mean(FWHM);
nub_C=sum(sum(A));
APPENDIX B: Images not used in the main text.

Images used for sinogram creation.
Very first mouse images:
Second mouse images:

Photographs of the system:
Nuclear Imaging Technology Laboratory.