MicroPET Scanner Characterization

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The development of MicroPET scanners, destined to rodents and small mammals, brings clear advantages in the clinical study of these animals, as well as in preclinical tests of medical products destined to human beings. The technology transfer between these and the human PET scanners is another advantage. In the High Energy Institute of the Vrije Universiteit Brussel, one of the members of the Crystal Clear Collaboration, a MicroPET scanner prototype - ClearPET1 - with the objective of its later commercialization. This scanner is this thesis’ study object. In it is made the description of the global architecture, of the detection modules, in which the photomultiplier tubes are the nuclear element, of the electronic modules associated with detection and of the data acquisition and treatment system. The axial profiles of sensitivity (ASP) were experimentally determined; the comparison between experimental results and simulations done in the Gate platform, showed the agreement between these. A new method, to calculate the scattered events fraction based on ASPs is presented. Also the results of the temporal resolution calculation are presented. The data analysis tools developed throughout the experimental work part of this thesis will be useful as a basis for the characterization of the new prototype, in a final stage: ClearPET2. The realization of improved simulations is needed to understand some unclear aspects focused in this thesis.

Keywords: MicroPET, Sensitivity, Scatter Fraction, Coincidence Time Resolution, GATE

I. INTRODUCTION

The MicroPET scanner prototype built at VUB, ClearPET 1, is the object of study of this thesis. The physical basis of PET as well as the general characteristics of a PET scanner are presented. The architecture of the ClearPET1 is described; this description includes the detection, the electronics and the Data Acquisition (DAQ) of the scanner.

The experimental part of this work is dedicated to the sensitivity characterization of the scanner. A new method of calculating the scanner scatter fraction is presented as well as the coincidence time resolution.

II. PHYSICS

A. Positron Emission

The positron emitted in a $\beta^+$ after annihilating with its antiparticle, the electron, given rise to the emission of two 511 keV photons in opposite directions. As a possible result of non-zero kinetic energy of the positron in the moment of annihilation, the angular deviation between the two photons is represented by a gaussian curve with an average of 180° and a FWHM of 0.5°.

These two photons are the physical observables in which PET techniques rely on. The photons interact with matter mainly by Compton Scattering, as this is the dominant interaction process at photon energies of $\sim$511 keV.

B. Isotopes

Being a functional imaging technique based on positron emission, the activity of a given part of the body is traced by the amount $\beta^+$ decays and consequent 511 keV gammas emission. It is thus necessary to introduce in the body elements decaying by $\beta^+$ like $^{18}$F, $^{11}$C or $^{15}$O refs 2 and 4. This is done by chemically linking these elements with organic molecules like serotonin or glucose. By linking an $^{18}$F atom to a glucose molecule, one obtains the radioactive compound $^{18}$F - FDG, the most widely used in oncology.

C. Photon Detection

To detect the photons emitted in the positron-electron pair annihilation, scintillator crystals are used. In PET inorganic scintillators are used; this type of scintillators have a high $Z_\text{eff}$ to achieve a good detection efficiency. A large efficiency is a desired characteristic.

The detection of scintillation light and its conversion to a current pulse is made by a Photomultiplier Tube (PMT). Scintillation photons hit the PMT photocathode and electrons are ejected from it by photoelectric effect; this process has an intrinsic efficiency: Quantum Efficiency. The photoelectrons are then successively multiplied in the PMTs dynodes until they reach the anode, where an electrical pulse is produced. The number of secondary photoelectrons is related with the voltage applied by eq. (1)

$$G = V^n$$

The energy resolution of an energy spectrum is measured with respect to a photopake. Because photopakes are Gaussian-shape like, rather than vertical lines, the energy resolution is given by the width at half height of the this gaussian. Thus the energy resolution is given by eq. (2)

$$R_{FWHM} = \frac{\Delta E_{FWHM}}{E}$$

III. EVENTS

The PET imaging techniques rely on the accurate determination of the two photons originated in the same emission, a coincidence.

Coincidences are distinguished between real coincidences, when the two detected photons are originated in the same annihilation; scatter coincidences, when, at least, one of the annihilation photons suffers Compton interaction(s) before being detected; random coincidence, when the two detected singles are originated in different annihilations. Fig. 1 illustrates this.

Due to the system's temporal resolution, a valid coincidence requires that photons are detected in opposite detectors, within a specified time window. This time window is typically of the order of nanoseconds. Random coincidences are estimated with a delayed time window process: a time window($\tau$) is open, not immediately after the detection of the first photon, but after a certain delay time ($d \gg \tau$). This takes to the loss of temporal correlation between the
two photons and instead of a possible true coincidence, a random coincidence is detected.

IV. PET SCANNER CHARACTERISTICS

A. Sensitivity

The sensitivity of a PET scanner expresses the ratio between detected coincidences and the total number of β⁺ decays that undergo pair annihilation given by eq. (3). It is strongly dependent on the detection efficiency as well as on the scanner geometry.

\[
sensitivity = \frac{N_{\text{detected}}}{N_{\beta^+}}
\]  

(3)

B. Noise Equivalent Count

Noise Equivalent Count expresses the relation between useful and noisy signal of a PET scanner, its expression is given by eq. (4)

\[
NEC = \frac{T^2}{T+S+2R}
\]  

(4)

Where T, S and R stand for true, scatter and random coincidences, respectively. NEC curves are expressed as a function of radioactivity, and allow to estimate the optimal relation between useful and noisy signal.

C. Spatial Resolution

Spatial Resolution translates the minimum distance between two points in the same image that a system can distinguish between. In a PET scanner this is particularly important in the sense that one is interested in detecting the possible smallest disease. Some factors contribute to the degradation of spatial resolution:

- the fact that the positron travels a finite distance between the production and annihilation spots.
- the non-collinearity of the emitted photons.
- the parallax error, this is due to the impossibility in determining the exact spot where a photon hits the scintillation crystal; this error is thus proportional to the crystal dimensions and in practice one reduces it by using more than one crystal layer with smaller dimensions.

D. Time Resolution

A PET scanner time resolution is a measure of how accurate the arrival time of one photon is determined. The determination of the coincidence time resolution is also done by computing the differences of arrival times of coincidence photons. This distribution is a shape-like gaussian, for which the coincidence time resolution can be measured as the FWHM of it. Time resolution and coincidence time resolution are related by eq. (5)

\[
\text{Coincidence time resolution} = \sqrt{2} \times \text{Time resolution}
\]  

(5)

V. CLEARPET1 SCANNER

ClearPET1 prototype was built at VUB and used for trials in Ghent University. It has an inner diameter of 143mm. Eight detection modules (cassettes) are disposed radially, being four of them diametrically opposing the other four.

A. Detection Modules

1. Scintillation Crystals

Two types of scintillation crystals are used: LSO and LuYAP. The dimensions of each individual crystal are 2x2x8 mm³. There is a total of 128 crystals mounted in two layers of an 8x8 Tyvek matrix. LSO crystals present a light yield (LY) about 4 times larger than LuYAP crystals. Setting a low discrimination value to the light pulses, would favor undesired low energy Compton events and multiple triggering events provoked by cross-talk. It is thus necessary to uniformize both crystal layers LYS. Three solutions are adopted to accomplish this:

- the LuYAP crystals light collection efficiency is raised by a factor 2, by directly gluing it to the photodetector window.
- LSO LY is decreased to a value 10% to 30% lower than LuYAP one by placing a sheet of Mylar in between both crystal layers
- LSO LY is increased by placing a light-reflecting paper in the outer face of LSO crystals.

2. Photo Multiplier Tubes

The Photo Multiplier Tubes (PMTs) used to detect scintillation light are Multi-Anode HAMAMATSU R7600-M64. They have a sensitive area of 18.1x18.1 mm² readout by a matrix of 64 cathodes, each having a surface of 2x2 mm² that matches the dimensions of the crystals surface, working thus as individual detector pixels. There are 64 individual anode outputs, as well as a common dynode output corresponding to the analog sum of the 64 individual pixels.

Phoswich matrix is the name given to the ensemble of both crystal layers and PMT.

3. cassettes

The dimensions of the cassette are 25x15x4 cm³. It is made out of aluminium and is the physical support to the detection and readout electronic modules. A box in the front of the cassette houses the light sensitive part of the scintillation crystals and PMTs; it is black in order to prevent these from direct light exposition.

B. Electronics

Each detection cassette contains the following components: two phoswich matrices, two decoder blocks, one FPGA, one slow control board and an optical link.
1. **Decoder Block**

Each decoder block consists of 64 comparators connected to PMT anodes, an address decoder of the anodes and a dynode signal preamplifier. The comparators are triggered if, at least, one anode signal exceeds a threshold value; this threshold value is common to the 64 channels and can differently be set for each PMT. When a trigger occurs the amplified dynode signal and the address(s) of hit pixel(s) are sent to the FPGA board.

2. **FPGA Board**

The FPGA board holds an FPGA and four free running 12-bit ADCs at 40 MHz. This 40 MHz is set by an external clock synchronous for all cassettes. When a trigger event occurs, 16 samples of the incoming dynode signal are saved.

The FPGA takes 700 ns to process each trigger event; this time is the biggest contribution to the dead time of the system. The 40 bytes of data are sent to a Data Acquisition computer via an optical link interface.

3. **Slow Control Board**

The slow control board is situated in the back part of each cassette; it is equipped with a microcontroller that adjusts High Voltage (HV) and threshold, individually, for each PMT. HVs are generated by DC-DC converters. HV and threshold settings are received from a Master PC, via a RS232 serial interface. Additionally, the microcontroller monitors the HVs and supply voltages as well as the temperature given by a sensor placed near the phoswich matrix.

4. **Optical Link**

In the top of the slow control board is placed a piggyback board with an optical transceiver unit but it is set to works only as a data transmitter; it sends 16 bits data words to a Slave PC at a rate of 10 MHz.

C. **Data Acquisition**

The DAQ of the scanner consists of one Master PC, two Slave PCs and a Data Storage PC. The communication between them is realised by socket connections at 1 GBit/s.

1. **Slave PC**

The data flow from from the eight cassettes is received by two Slave PCs. Each Slave PC holds two interface boards with two I/O cards each. Each I/O card holds the same piggyback boards as the optical link, this time using the receivers only. The 32-bit port of each I/O card is configured as two 16-bit independent ports; one card is then able to receive data from two cassettes. The data transfer made up to a rate of 450 × 10⁶ events/s.

For each event received from a cassette the Slave PC processes the raw data and computes the following:

- **Energy**
  
  Energy of the pulse is given by the sum of the 16 digitized pulse samples, after pedestal subtraction.

- **Time Mark**
  
  A straight line is fitted into the two points for which the slope is maximum; the intersection of this line with the baseline of the pulse is considered the new event time mark. This method improves the scanner’s temporal resolution from 25 ns to 4.2 ns [11].

**DOIs**

The depth of interaction information, i.e., the information whether the crystal layer where the trigger event was produced in LSO or LuYAP layer is determined using a method called Pulse Shape Discrimination, based on the presence of a slow decay component of LuYAP scintillation pulse. This PSD method has a reliability of 97% [8].

2. **Master PC**

The Master PC is responsible for controlling all the scan processes. It runs a LabView application that manages a Graphical User Interface (GUI) allowing to control the parameters of the acquisition such as time of acquisition, bed position and gantry rotation.

VI. **RESULTS**

A. **Sensitivity**

In the sensitivity characterisation of the scanner one first presents the comparison between simulated and measured data for the Axis Sensitivity Profile of the scanner 2.

![Full Scanner Sensitivity](image)

**FIG. 2:** PMTs measured singles rate compared with simulation. Left: level 0 PMTs. Right: level 1 PMTs.

Simulated and measured sensitivity values are not in agreement; the highest sensitivity points are 0.69% and 0.43% for simulation and measurement respectively; this means a loss of ~38% in measured sensitivity. Simulated total sensitivity is 42% higher than measured one.

Measured curve also presents an asymmetry relative to the y axis and an asymmetry between the first four and the last four measured z positions.
1. PMT singles rate

For each PMT the measured and simulated singles rate were calculated by eq (6)

\[ \text{rate} [s^{-1}] = \frac{\text{singles}}{\text{acquisition}} \]  

Fig. 3 shows the singles rates for each PMT along the z axis of the scanner.

FIG. 3: PMTs measured singles rate compared with simulation. Left: level 0 PMTs. Right: level 1 PMTs; for clarity of visualisation, only one simulated PMT is shown, as simulated single count rate per PMT is practically equal.

One can see that, for the four PMTs of cassettes 11 and 12, there are bad data points, between 18 mm and 24 mm. Indeed, the log files of the measurement show that between those specific positions, there are no counts for these specific PMTs, due to an error in data acquisition.

The real PMT that agrees best with simulation is PMT 9 of cassette, with a 91% ratio. The PMT with a worst agreement is PMT 1 of cassette 11, with a ratio of 56%. The average of all the ratios is 75% ± 11%.

The bad data points previously noted explain the asymmetry in the measured curve in fig. 2.

In order to explain this average difference of 25% in singles rate between simulation and measurements, some issues were identified as possible factors of disagreement: factors where simulation doesn’t include some phenomena taking place in the real system, and also factors where simulation does not take into account the variations on performance of components of the same type, specifically the PMTs.

a. Real PMT Characteristics

In simulation PMTs thresholds are set to a sharp defined value; in this specific work this value is set to 250 keV. This precision is not possible in the real system due to the energy calibration method used. The simulated energy resolution is 22.9%.

The average measured threshold level is 219 keV ± 16%. The average energy resolution is 34.6% ± 5.4%.

b. LSO Background

LSO crystals contain approximately 2.6% of \(^{176}\)Lu [10], a natural occurring radioisotope that is a γ emitter. Its influence on single count rates has been measured and is not negligible [9]; LSO background is not simulated. This background radioactivity accounts with ∼ 10% to the measured singles count rate.

c. Position and Energy Errors

During measurements, errors in determining the index of the pixel hit, fars and errors of position, and errors of energy are expected to happen. In the simulation these errors are not included. The log files of the acquisition show an average of 10.5% of errors over the total single count.

We assume that the bad results between the simulated and measured count rates of PMTs shown in fig. 3 have its origin in the following reasons:

- The contribution of the LSO background that underestimates the simulation count rates by ∼ 10% is not negligible.

- The average threshold level of real PMTs, 219 keV, which is good result compared with the 250 keV threshold level set in simulation; its dispersion of ∼ 16% is expected, giving the method used to experimentally set it, explained before.

- The contribution of the bad events to the loss of counts in the real system, although its origin is not clear, can be quantified; for each PMT there is a fairly constant percentage of this error, over all the measured z positions. In average ∼ 11% of the singles are bad events; these are not accounted in simulation.

- In spite of not having influence in the singles count rate, an over-estimated average of 34.5% is fairly worse than a energy resolution of 22.9% for simulation.

For the characterisation in sensitivity of the scanner, the previous discussion will be taken into account; because setting the individual characteristics of each PMT is not feasible in simulation, the method used is to adapt the simulated to the measured data: The simulated count rate will be scaled to its respective PMT in the real system; the scaling factors shown are defined individually for each PMT; each one of these corresponds to the measured/simulation ratio, averaged over all the z positions. In it is included the contribution of all the disagreeing parameters discussed before.

In the coincidence sorting algorithms for simulated data, for the specific PMT pairs for which coincidences are detected, a fraction of the singles events are rejected, via a random selection, according to the singles rate scaling factor for each PMT.

2. PMT Pair Coincidence Sensitivity

The following analysis will be the characterisation in sensitivity for coincidences of a PMT pair, from opposite cassettes. Only coincidences between same index PMTs (PMT0-PMT0 or PMT1-PMT1) are considered.

Fig. 4 shows the sensitivity profiles for all same level PMT combinations for all pair of opposite cassettes.

FIG. 4: Simulated and measured sensitivity for PMT pairs. Blue: simulation PMTs index 0. Red: measurement PMTs index 0. Green: simulation PMTs index 1. Black: measurement PMTs index 1. Only cassette pairs 1-11 and 2-12 are shown.

3. Cassette Pair Coincidence Sensitivity

The sensitivity to coincidences for all pair of opposite cassettes will now be analysed; all coincidences for a specific cassette pair are accepted.

In fig. 5 the sensitivity profiles for the four pair of opposite cassettes are shown; z position for measured data is corrected for each cassette pair with the respective peak deviations.

The lateral peaks of the profile show the contribution of same index PMT sensitivity shown in fig. 4; The central peak expresses the sensitivity for the coincidences occurring between PMTs of different index.

Left and right peaks of each profile show an expected behaviour when compared to the respective peaks of fig. 4: there is a maximum difference of 4% between respective left and right peak ratios.
The averaged central peak and total sensitivity ratios are, respectively, 0.96±0.07 and 1.04±0.11.

These numbers shows a consistent agreement in cassette pair sensitivity with the results for PMT pair sensitivity.

4. Full Scanner Sensitivity

The sensitivity of the full scanner will now be recalculated. Results for the simulated and the measured sensitivity profiles are shown in fig. 6.

A good agreement between measured and simulated total sensitivity is seen, with a measured to simulation ratio of 96%. The central (z=0 mm) position, corresponding to the point of the scanner’s maximum sensitivity shows an improvement of the agreement between measurement and simulation, with ratio of 91%.

5. Scatter Fraction

In this work a method of estimating scatter fraction using sensitivity profiles will be presented. The following points have to be considered when using this method:

- to calculate a full scanner sensitivity coincidences from all PMT combination are accepted; a fraction of this coincidences are due to scattered events in the scanner’s material, such as the metallic parts of the rotation gantry, the cassettes and the animal bed.

- the source is positioned at the central line of the scanner (x = 0 y = 0), so that the scattered coincidences are the ones occurring in non opposite cassette pairs.

- when calculating cassette pair sensitivity, only coincidences from the specific cassette pairs are accepted.

Taking into account the previous considerations, one concludes that the scattered coincidences are the difference between coincidences detected for the full scanner’s sensitivity (fig. 6) and the sum of coincidences detected for the cassette pair sensitivity profiles (fig. 5).

In fig. 7 is shown the full scanner sensitivity profile and the sum of the four individual cassette pair sensitivity profiles.

The number of scattered coincidences is then the difference between red and blue curves. In fig. 8 (left) this difference is expressed in sensitivity; in fig. 8 (right) is shown the scatter fraction.

\[
SF[\%] = \frac{\text{scattered}_\text{coin}}{\text{total}_\text{coin}}
\]  

(7)

Fig. 8 (left) shows a fairly uniform distribution of scattered coincidences along the z axis, for measured data, while simulated one shows a similar shape profile to the scanner sensitivity profile. This seems to indicate a dependency on the scanner geometry for the simulated data. This can be explained by the fact that, in simulation, structural elements such as the bed or the metallic rotation gantry are not modeled. The scattered events occurring in these elements, in the real system, can explain the totally different distribution of scattered events for simulated and measured data along the FOV of the scanner.

Fig. 8 (right) shows a good agreement in shape between scatter fraction curves, despite the fact that the profile of the number of scattered coincidences is very different for measurement and simulation.

Scatter fraction is minimum in the centre of the FOV with 21% and 16%, respectively for simulation and measurement. In the extreme points of the FOV it can go up to 60% both for simulation and measurement; this SF curve would eventually reach 100% for even more extreme positions of the FOV, as the solid angle for real coincidences tends to zero.

a. Scatter Fraction Correction

Assuming that in the simulation the scattered events are well modeled, and that the difference with measurements is due to the fact that the structural elements referred before are not modeled, we can apply a correction to the full scanner’s sensitivity profiles of both measurement and simulation: each sensitivity profile will be corrected for the corresponding fraction of scattered events. With this correction one obtains the full scanner’s sensitivity profile for true coincidences shown in fig. 9.
The results for determining the coincidence time resolution of the scanner will be presented now.

Coincidence time, \( \Delta t_{\text{cor}} \), is defined as the difference between the arrival times of two coincidence photons. The arrival time mark is calculated as explained in Sec. 3.4. The photon's arrival time distribution has a Gaussian shape, implying that \( \Delta t_{\text{cor}} \) distribution also has a Gaussian shape.

Fig. 10 shows \( \Delta t_{\text{cor}} \) distribution, for four PMT pairs combination; the fact that these distributions are not centred in 0, is due to the different transit times in PMT and/or electronics [3]. The average position of the distribution is presented as well as the time resolution for each distribution.

All of the above distributions show an asymmetry in the tails of the Gaussian curve; this asymmetry is related with the difference of incoming pulse shapes [7].

By summing the distributions of all the PMT pair combination of a pair of opposite cassettes, one obtains the \( \Delta t_{\text{cor}} \) for a cassette pair; also the different delays presented for each distribution are taken into account, as each distribution average is shifted towards zero. Fig. 11 shows the summing of the four distributions of one cassette pair; the LSO and LuYAP resolutions are also plotted.

One can see that LuYAP energy resolution is systematically worse than LSO one. The explanation for this fact is related with the difference in determining the arrival times of pulses with similar shapes, but with different amplitudes [7]. Pulses with a lower amplitude, this is the case if LuYAP and LSO LYSs are compared, show a higher dispersion in determining the arrival time, leading to worst time resolutions.

The global coincidence time resolution of the scanner is 5.34 ns, while time resolutions for LSO and LuYAP layers are 5.07 ns and 5.61 ns, respectively. Using eq. (5) one obtains a time resolution of 3.77 ns.
The results obtained for the sensitivity of the scanner can be considered satisfactory. The good agreement between measured data and GATE simulations could be observed for PMT pair, cassette pair and full scanner sensitivity. The measured and simulated full scanner sensitivity for the highest sensitivity point were 0.36% and 0.35%, respectively.

Not only the results were satisfactory but, more important, the methods used for characterising the scanner's sensitivity lead us to a better understanding of the scanner. One was able to evaluate the different performances of the nuclear component of the detection system: the photomultiplier.

The energy resolutions showed a big deviation relatively to simulation: the best real system energy resolution was significantly worse than the simulated one, with respective values of 28.1% and 22.9%. The measured threshold energies of the PMTs were in a good agreement with simulation, with an average value of 2.49 keV, while simulated threshold was of 2.50 keV. The influence of LSO background was well determined: it contributed not only to an increase in the measured singles count rate, but also had influence in the energy resolution determination. In the inverse way, the amount of bad events contributed to a decrease in the measured singles count rates; the origin of these errors in the real system is not clear, but its contribution to the measured singles decrease is well known for each PMT. A much lower contribution to the measurement/simulation disagreement was detected: small deviations in the positioning of PMTs were measured, as well as the existence of a systematic error of 0.86 mm in determining the real position in measurements.

A new method of determining the scatter fraction using sensitivity profiles was presented. The results show a similar behaviour between measured and simulated scatter fraction. The variation of the SF between the centre and the extreme positions of the FOV was of 24% to 60% and 16% to 50% for simulation and measurement, respectively.

All the previously described factors will be useful in future work on the second version of the ClearPET; ClearPET2 differs from ClearPET1 in the crystals height and in the number of PMT per cassette: it will have 8 mm long crystals and 4 PMTs per cassette. In spite of that, the methods used to calculate PMT energy resolutions and thresholds remain valid in the new scanner.

The future simulations relative to the new scanner can also be improved, taking into account the issues shown previously and that were not modeled in simulations used in this work.

The measured global time resolution of the scanner is 5.34 ns. The time resolutions of LSO and LuYAP crystal layers were also calculated and are 5.07 ns and 5.61 ns, respectively; the lower time resolution of LSO compared to LuYAP was expected, given the difference in the light yield of both crystals.

The time resolution between PMT pairs were also calculated; an unexpected asymmetry in the coincidence time distribution was detected, but its origin was related with the difference in pulse shapes.