Initial results from a dual head PET system, suitable for small animal imaging

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***Abstract*: The aim of this work is the development and evaluation of a dual head PET system suitable for small animal imaging. This system is the results of the collaboration between the Department of Medical Instruments Technology, the Institute of Radioisotopes and Radiodiagnostic Products of N.C.S.R. "Demokritos" and the Detector and Imaging Group of Jefferson Lab (US). The system is based on two LSO crystals, coupled to two H8500 PSPMTs and its field of view is 5×5cm. Readout is carried out using FPGA electronics. At this phase the system is suitable from coincidence planar imaging, Results using phantoms are provided; the spatial resolution as a function of distance is measured using capillary phantoms. The effect of data acquisition parameters on raw signals and images are given. Finally, initial results from a mouse injected with FDG are shown. This is the first dedicated PET prototype that has been developed in Greece and it will be used in molecular imaging studies in small animals.**

I. Introduction

Positron emission tomography (PET) is a molecular imaging technique based on the use of compounds labeled with positron emitter isotopes; when positrons traveling in tissue meet a free electron they annihilate, producing a coincident gamma ray pair that can be externally detected by a PET scanner. PET exploits the annihilation of positrons and electrons into simultaneous back-to-back 511-keV photons to achieve nuclear imaging in a way similar to SPECT systems. The positron is the positively charged antiparticle of the electron. Unstable nuclei that are proton rich may decay by positron emission. If the two detectors are in coincidence, the assumption is that an annihilation occurred along the line that connects them, referred to as the "line of response" (LOR).[1,2]

The main sources of error in preclinical PET imaging, where detectors ring is narrow and no sufficient body movement takes place, are the following. The positron can move a substantial distance before colliding with an electron. Furthermore, if the annihilation photons are noncolinear (i.e., off of 180° from one another), the detected LOR would not correspond to the site of annihilation. Two additional problems limiting resolution are Compton scatter and random coincidences. Scatter will result in the LOR no longer passing through the true annihilation location, while random coincidences occurs at high count rates where two photons from two different events are detected in coincidence. The LOR will not be representative of either event in that case.[1,2]

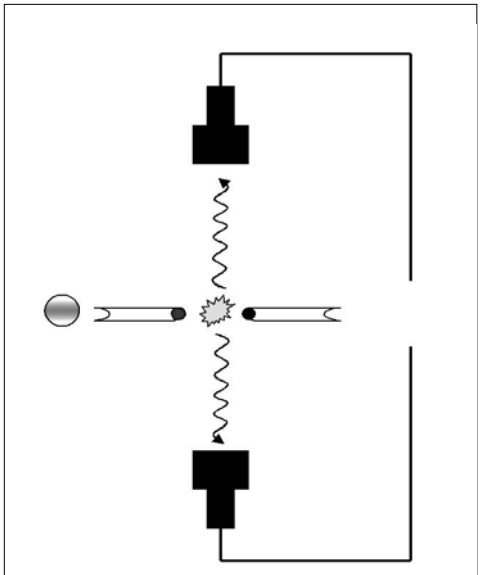

Illustration 1: Schematic diagram of PET basic principles

The most widely used PET tracer in oncology is 2-18Fluoro-2-deoxy-glucose (FDG) [3]. The rationale behind its use is the increased rate of glucose consumption in malignant tissues, due to an increase of

glycolysis, and of the number of glucose transporters expressed on malignant cells. After injection, FDG is transported by facilitated diffusion into neoplastic cells where it is phosphorylated by hexokinase and subsequently is trapped as it is not a substrate for the subsequent enzymatic driven pathways for glucose metabolism. As the neoplastic cells accrue larger amounts of FDG due to their increased metabolism, increased activity is detected that delineates the hypermetabolic tumour from the surrounding normal tissues.

Since its first application in brain imaging, PET has been increasingly used for its ability to detect primary malignant tumours, but also for its ability to detect both regional and distant metastases, distinguish benign from malignant tissue or recurrent cancer from treatment-related scarring, and document response to therapy [3].

Recently the growing interest in pre-clinical imaging studies, both in biological and medical basic research, and in pharmaceutical industry, has recently induced the world-leading manufacturers of medical image equipment to invest in this market. The result was the rapid development of the dedicated small animal PET scanners. The term small animals mainly include rats and mice. Small animal imaging is used not only for oncological studies but also for the non-invasive assessment of biological processes. In those applications high spatial resolution and sensitivity are required [4].

In this work the first small animal PET scanner in Greece is presented. A partial evaluation in terms of FWHM and sensitivity. Also initial results from a mouse injected with FDG twice with different acceptance angles and selected z-planes. The acceptance angle defines the maximun detection distance from the center of the field of view where the two gamma photons can accepted as a valid event.

II. Methods

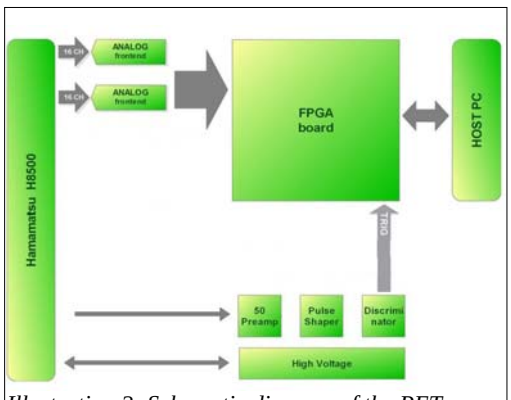

Illustration 2: Schematic diagram of the PET system

The small animal PET scanner is currently suitable only for planar imaging; a rotating gantry has been ordered and will allow the acquisition of projection data. It comprises of two 20×20 pixel LSO crystals, 2.2×2.2mm in size and 2.5×2.5 with septa, coupled to two Hammamatsu H8500 PSPMTs [5]. The PSPMTs have dimensions of $52\times52cm^2$ and effective area of $49\times49cm^2$. The number of pixels of the anode is 64 (8×8), but it is reduced to only 8 X plus 8 Y channels, in order to decrease electronics complexity [6]. Those 16 signals are used for the production of the final image without significant position accuracy loss. The PSPMTs window is made from borosilicate glass, the photocathode material is bialchali and its spectral response range is 300 to 650 nm, with peak at 420 nm.

Illustration 3: The compact H8500 PSPMT

The signals from the PSPMTs are preamplified. The 16 channels from each PSPMT go to the ADCs in order to be processed from an FPGA before they enter to a host PC. One more signal cable from each tube is used for the coincidence detection. These two signals enter into a trigger box. Here an "AND" logic circuit is used to detect the true annihilation events and exclude randoms. The entrance of the two pulses in the circuit has to be done within a certain time window, and their amplitude should exceed a proper value (threshold). The output from this circuit also enters to the FPGA processor. Further processing of the radioisotope distribution takes place in the host PC using a GUI designed in the Kmax environmet (Sparrow Corp., Port Orange, FL, 321), using Java.

System calibration is carried out using point sources. As a first step energy thresholds in both heads and optimal high voltage have to be adjusted. Following, a Look Up Table (LUT), which will links each pixel to a unique crystal, is constructed. Then energy peak channels in each crystal pixel (in both heads) have to be defined. System has been evaluated

using capillary sources (1.1mm inner diameter and 8cm long, as well as point-like sources, filled with FDG solution.

III. Results

In illustration 4 a map of the LSO crystals is shown. The 20x20 matrix is clearly mapped without any major distortions. In order to be archived this a Look Up Table (LUT) has to be constructed which will link each pixel to a unique crystal. This map doesn't contain information about the true annihilation events, it maps all the photons which are detected on each head. The non uniformity in this image is explained by the fact that the source was a capillary placed in the upper part of the field of view.

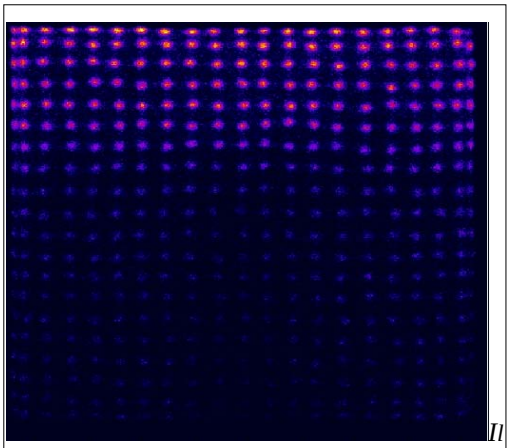

Illustration 4: The pixel map of the 20x20 LSO crystal

Illustration 5 is an uncorrected spectrum in one of the two heads. It is just the sum of all the pulses from all detected photons without any position correction. It is produced from a spot source located near the center of the FOV. This is the reason why most pulses are at high channels.

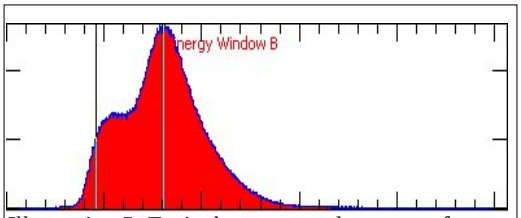

Illustration 5: Typical uncorrected spectrum from spot source located near the center of the FOV.

Illustration 6 shows a spectrum that has been corrected for photons that are detected at the PSPMT edges. Its clear that the low energy part has less counts. The peripheral true events are now corrected and added to the peak channel.

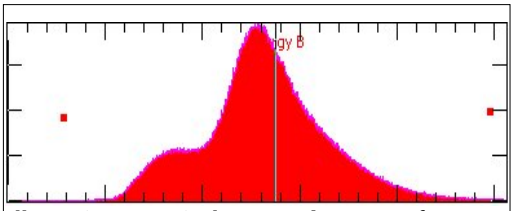

Illustration 6: Typical corrected spectrum from a spot source located near the center of the FOV.

Initial results using capillaries tubes showed that the FWHM for 70mm distance between the two heads is 2mm wide for 10^{o} acceptance angle. For smaller degrees the apparently better spatial resolution is an artifact.

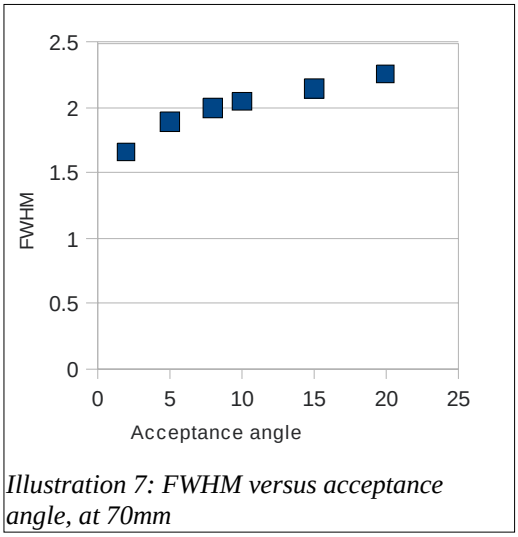

Illustration 7: FWHM versus acceptance angle, at 70mm

For 50mm head distance the most appropriate acceptance angle would be ~8^{o}. It is obvious that smaller distance would require smaller acceptance angle.

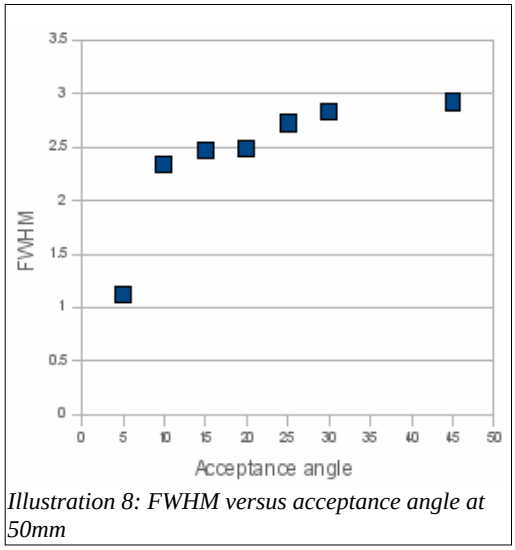

Illustration 8: FWHM versus acceptance angle at 50mm

Rather interesting are the results in illustration 9, which shows how the FWHM

changes versus the z-field location. The head separation distance is 70mm, so the central z-plane (0 distance) is at 35mm and the acceptance angle 5°. As it can be seen the spatial resolution is better for the z-planes which are at 30mm. As the z-plane of interest is moving closer or further the FWHM is greater because it moves out of the focus

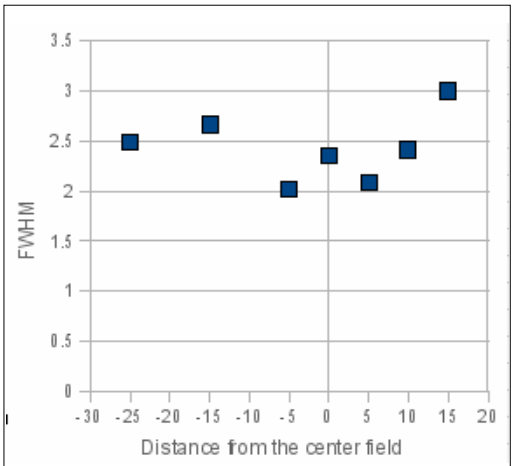

Illustration 9: FWHM versus the z-plane location

plane.

In Illustration 10 a planar image of a mouse injected with FDG is shown. The mouse has been sacrificed 30 minutes post injection. Head distance was 80mm and acceptance angle was 35 degrees. The three successive images show radiopharmaceutical's distribution at the central plane (0mm) as well as at positions -5mm and -10mm respectively.

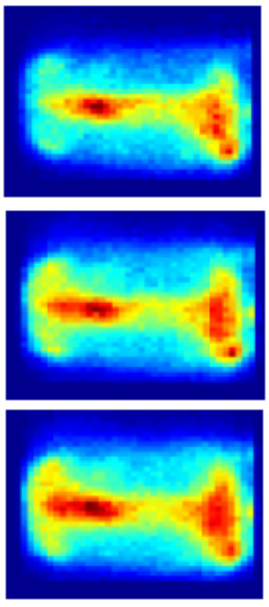

Illustration 10: Tree successive images that show FDG distribution in a small mouse bones at the central plane (0mm) as well as at positions -5mm and -10mm respectively.

IV. Discussion, Conclusions.

The initial results of this systems performance show that it is suitable for mouse imaging, since it offers a spatial resolution of 2mm. Current work includes a) data acquisition optimization, b) software optimization, c) optimization of hardware set up. More specifically, studies with point and capillary sources aim to determine optimal acquisition settings. In addition, software modifications are carried out in order to optimize data processing as well as image manipulation in animal studies. An important task is the construction of a stable base that will mount both heads and the objects-to-be-imaged, so that all experiments will be reproducible. Future work includes mounting the two heads on a rotating gantry [7], which will allow acquisition of projection data and PET reconstruction.

The aim of this collaboration is the use of system in the evaluation of novel PET radiopharmaceuticals. As a first step As-77 based derivatives will be studied. This is the first small field of view PET system in Greece and it is expected to initiate national PET radiopharmaceuticals research. Moreover, it can be used to study breast phantom, since dedicated Positron Emission Mammography (PEM) cameras are based on this principle. Finally, this system is open and it can be used as well for teaching purposes both for data acquisition and raw data processing.

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