A digital data acquisition scheme for SPECT and PET small animal imaging detectors for Theranostic applications

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Abstract. Nanoparticle based drug delivery is considered as a new, promising technology for the efficient treatment of various diseases. When nanoparticles are radiolabelled it is possible to image them, using molecular imaging techniques. The use of magnetic nanoparticles in hyperthermia is one of the most promising nanomedicine directions and requires the accurate, non-invasive, monitoring of temperature increase and drug release. The combination of imaging and therapy has opened the very promising Theranostics domain. In this work, we present a digital data acquisition scheme for nuclear medicine dedicated detectors for Theranostic applications.

1. Introduction
Molecular imaging of cancer using nano-materials is potentially an important tool in diagnosis, therapy and drug delivery [1]. Radiolabelled magnetic nanoparticles can penetrate biological barriers, carry drugs on the target site, while minimizing dose in other organs. Their magnetic properties allow them to be heated and either allow controlled drug release and/or transfer heat to cancer cells, thus induce a hyperthermic effect. Magnetic hyperthermia treatment (MHT) is a cancer therapy that relies on the heat produced by magnetic nanoparticles under alternating current magnetic field (ACMF), and it has the potential to realize a local, scarless and economical treatment with fewer side effects [2]. On the other hand, when nanoparticles are radiolabelled it is possible to image them, using standard molecular imaging Single Photon Emission Computed Tomography (SPECT) or Positron Emission Tomography (PET) techniques. The combination of imaging and therapy has opened the very promising Theranostics domain. Simultaneous nuclear imaging during hyperthermia can provide insights in the biological process that occur when nanoparticles are heated. In this way it is possible to monitor the successful organ/tumor targeting, drug release and/or real time response to therapy.

In this work we present a flexible, cost-efficient Field Programmable Gate Arrays (FPGA) based data acquisition scheme for SPECT and dual head PET small animal imaging detectors designed for Theranostic applications. The construction of cost efficient detectors, which can support simultaneously SPECT and PET imaging would provide an efficient tool in the field of Theragnostics.
2. Materials and Methods

2.1. Detectors and front-end electronics

The SPECT camera used for evaluation of the proposed data acquisition scheme consists of a pixelated \((1 \times 15 \text{mm}^3)\) NaI(Tl) scintillator (SaintGobain, France) with an active area of \(97.4 \times 44.8 \text{mm}^2\) coupled with optical grease BC-630 to a pair of two square H8500 flat-panel PSPMTs (Hamamatsu, Japan) with external dimensions of \(52 \times 52 \times 34 \text{mm}^3\). The high voltage was set to -965 V, for 140 keV excitation. A general purpose parallel-hole lead collimator is used (Nuclear Fields Co, Netherlands), with hexagonal holes of 1.2 mm inner diameter and 0.2 mm thick septum walls. Its height is 25 mm, with an active area of \(52 \times 105 \text{mm}^2\).

For PET evaluation two detector modules with an active area of \(100 \times 50 \text{mm}^2\) were used. Each one consists of a pixelated \((2 \times 2 \times 5 \text{mm}^3)\) BGO scintillator (Hilger Crystals Ltd, UK) coupled with optical grease BC-630 to a H8500 PSPMT. The high voltage was set to -930 V and -910 V, respectively, for 511 keV excitation.

The same analog front-end scheme was used for both SPECT and PET detectors. The 128 output signals of each detector were reduced to 4 position signals through a Symmetric Charge Division (SCD) Circuit [3]. Four custom pre-amplifiers at the end of the resistive chain shape the position signals, taking into account the analog to digital conversion (ADC) sampling rate.

2.2. Digital readout electronics

The position signals are continuously sampled by a 12 bit octal channel free running ADC with up to 65 MHz sampling rate (ADS5282EVM, Texas Instruments, US). Four channels at 50 MHz sampling rate and eight channels at 65 MHz sampling rate are used for SPECT and PET acquisition, respectively. The digitizer is connected to a Xilinx Spartan 6 LX150T FPGA (Avnet Inc, US) via a FMC-LPC connector. The platform also contains a 128 MB DDR3 SDRAM component memory and a gigabit Ethernet, which are used for temporary data storage and transmission.

![Figure 1. Block diagram of the general data acquisition system architecture.](image-url)
registers implemented inside the FPGA, of appropriate length to ensure that complete amplified pulses can be stored there.

2.2.1. \textit{SPECT DSP module}. When the instantaneous energy of the detector (sum of 4 output signals) exceeds a predetermined digital threshold, implying the arrival of a photon, a finite state machine (FSM) is triggered. A delay circuit is activated, in order to shift the remainder samples of pulses inside the registers and at that time the FSM enables its integration. While recorded data are being processed and the information of interest is written to the external memory, a second set of registers are ready to accept the next potential event.

2.2.2. \textit{PET DSP module}. When the sum of the 4 output signals of one detector exceeds a predetermined digital threshold, implying the arrival of a photon, a finite state machine (FSM) is triggered. To determine if this photon was produced by an annihilation process, the FSM opens a time window equal to 60 ns, in order to allow a possible detection of a second photon at the opposite detector. If the energy of a second photon exceeds the digital threshold, a delay circuit is activated, in order to shift the remainder samples of both pulses inside the registers. Then the FSM enables the integration of the pulses, as well as computing a timestamp for each event recorded from the detectors. A digital version of the constant fraction discriminator (CFD) algorithm was implemented, in order to achieve a time resolution higher than the sampling period. Otherwise, the FSM waits for a time window equal to the amplified pulses duration (985 ns) and restarts. While recorded data are being processed and the information of interest is written to the external memory, a second set of registers are ready to accept the next potential coincident event. The coarse coincidence gate for preselection was set to 60 ns because of the relative slow rise time (150 ns) of the amplified BGO pulses.

2.3. \textit{Data transmission and post processing}
For every 1000 events stored in the memory, an interrupt signal occurs by the DSP module that triggers the transmission of data to a PC via Ethernet using User Datagram Protocol (UDP). For SPECT, the energy and the Cartesian coordinate that correspond to the position of an event can be determined from the four signals [3]. For PET acquisition, coincidence data are grouped to projections using the non-iterative Focal Plane Tomography (FPT) algorithm [4].

2.4. \textit{Performance evaluation}
Point and capillary (6 mm length, 0.6 mm inner diameter) $^{99m}$Tc and $^{68}$Ga sources were used for performance evaluation. $^{99m}$Tc sources were used to acquire planar scintigraphic data from the SPECT camera, while $^{68}$Ga sources were used to acquire data from the dual head PET detector in coincidence mode. The point sources were used for energy and timing resolution measurements, while the capillaries for spatial resolution and sensitivity. Performance evaluation was based on previously published literature [5], [6].

3. \textit{Results}
(Table 1) summarizes the measured parameters of interest. The spatial resolution for planar scintigraphy was measured to be 1.9 mm upon the collimator and $\sim$3 mm at the 10 - 20 mm distance, where the mouse organs are usually located. The mean value of Spatial Resolution (containing x and y plane) for the PET system was calculated to be 3.5 mm. Timing resolution for PET was measured to be 8.2 nsec (figure 2). The energy resolution measured through the normalized energy spectra is 19.2 % and 22.3 % (average) for planar scintigraphy and PET, respectively. The sensitivity was measured to be 80 cpm/$\mu$Ci using an $\pm$ 20% energy window for the planar scintigraphy system. PET absolute sensitivity was measured to be 0.6 % for an
energy window of 300-700 keV. Two capillaries at a distance of 2 mm and the corresponding profile in planar scintigraphy imaging are imaged in figure 2 (middle). Similarly, two capillaries at a distance of 4 mm are imaged in figure 2 (right). It can be seen that the two capillaries are clearly distinguished in both occasions, as expected.

Table 1. Performance parameters

| PARAMETER                | Planar scintigraphy | PET       |
|--------------------------|----------------------|-----------|
| Spatial resolution       | 1.9 mm (upon the detector) | 3.5 mm (mean) |
| Timing resolution (FWHM) | -                    | 8.2 nsec  |
| Energy resolution        | 19.2 %               | 22.3 % (average) |
| System sensitivity       | 80 cpm/µCi           | 0.6 % (absolute) |

Figure 2. Measured coincidence timing histogram for PET imaging (left), Two capillaries at a distance of 2 mm and the corresponding profile in planar scintigraphy imaging (middle), Two capillaries at a distance of 4 mm and the corresponding profile in PET imaging (right).

4. Conclusions

A prototype scheme for data acquisition from small animal imaging SPECT and PET detectors based on a single reprogrammable platform has been developed and evaluated. Performance evaluation in planar scintigraphic imaging is similar to the one obtain by our group previously [5], using the same camera and different data acquisition architecture. As far as concern dual head PET imaging, performance is comparable to similar architectures previously published [6], [7]. The presented work is the first step in the construction of a PET/SPECT system specially designed for simultaneous nuclear imaging during hyperthermia providing the possibility to monitor the successful organ/tumor targeting, drug release and real time response to therapy.

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