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FPGA Electronics for OPET: A Dual-Modality Optical and Positron Emission Tomograph

Ali Douraghy [Student Member, IEEE],

UCLA David Geffen School of Medicine, Crump Institute for Molecular Imaging, Los Angeles, CA 90095 USA (adouraghy@mednet.ucla.edu)

Fernando R. Rannou [Member, IEEE],

Department de Ingenieria Informatica, Universidad de Santiago de Chile, 7251657 Santiago, Chile (rannou@diinf.usach.cl)

Robert W. Silverman [Senior Member, IEEE], and

UCLA David Geffen School of Medicine, Crump Institute for Molecular Imaging, Los Angeles, CA 90095 USA (bsilverman@mednet.ucla.edu)

Arion F. Chatziioannou [Member, IEEE]

UCLA David Geffen School of Medicine, Crump Institute for Molecular Imaging, Los Angeles, CA 90095 USA (archatzioann@mednet.ucla.edu)

Abstract

The development of a prototype dual-modality optical and PET (OPET) small animal imaging tomograph is underway in the Crump Institute for Molecular Imaging at the University of California Los Angeles. OPET consists of a single ring of six detector modules with a diameter of 3.5 cm. Each detector has an 8×8 array of optically isolated BGO scintillators which are coupled to multichannel photomultiplier tubes and open on the front end. The system operates in either PET or optical mode and reconstructs the data sets as 3D tomograms. The detectors are capable of detecting both annihilation events (511 keV) from PET tracers as well as Single Photon Events (SPEs) (2–3 eV) from bioluminescence. Detector channels are readout using a custom multiplex readout scheme and then filtered in analog circuitry using either a γ -ray or SPE specific filter. Shaped pulses are sent to a Digital Signal Processing (DSP) unit for event processing. The DSP unit has 100 MHz Analog-to-Digital Converters on the front-end which send digitized samples to Field Programmable Gate Arrays which are programmed via user configurable algorithms to process PET coincidence events or bioluminescence SPEs. Information determined using DSP includes: event timing, energy determination-discrimination, position determination-lookup, and coincidence processing. Coincidence or SPE events are recorded to an external disk and minimal post processing is required prior to image reconstruction. Initial imaging results from a phantom filled with ^{18}F FDG solution and an optical pattern placed on the front end of a detector module in the vicinity of a SPE source are shown.

Keywords

Bioluminescence; optical imaging; positron emission tomography; small animal imaging

I. Introduction

OPET is a dedicated murine model dual-modality imaging tomograph, capable of detecting both annihilation events (511 keV) from PET tracers as well as Single Photon Events (SPEs) (2–3 eV) from bioluminescence. OPET can be a useful tool for research involving simultaneous optical and PET signal imaging such as investigating two concurrent biological processes with two separate probes, or using fused protein molecular reporter probes that can co-express both optical and PET signals with the same promoter [1]. By combining these two modalities into a single imaging system, biological researchers will have at their disposal a novel tool to aid in studies of animal disease models, with the overall goal of translating the results of this research into the clinical domain.

The OPET system demonstrates that the same photomultiplier based detector can be used to detect γ -rays as well as bioluminescence SPEs. The OPET detector concept [2], and simulated PET system performance [3] have previously been described in more detail.

II. Materials and Methods

A. Signal Processing Components

OPET has a single ring of six detector modules with a diameter of 3.5 cm. The proposed full-ring signal processing chain (Fig. 1) consists of: Detector Modules, Analog Electronics, and a Digital Signal Processing (DSP) unit. The system can currently operate in *either* PET *or* SPE (optical) mode. For each mode, DSP algorithms were developed for event processing.

Readout channels from the detector modules are filtered in analog circuitry using an analog shaping circuit switchable between PET *or* SPE modes. The filtered channels are then sent to a DSP unit for digitization and event processing. For each mode, either PET or SPE, the user selects the correct analog circuit and loads the respective DSP algorithm onto the DSP unit. Processed events are written to an external Ethernet disk and minimal post processing of the data is required prior to image reconstruction.

In this work, results from a two-detector version of the PET DSP algorithm as well as from a single-detector version of the SPE DSP algorithm are presented and discussed.

B. Detectors

Each OPET detector module (Fig. 2) consists of an 8×8 array of Bismuth Germanate (BGO) scintillators (Proteus Inc., Chagrin Falls, OH) coupled to a 64-channel R5900-02-M64 multi-channel photomultiplier tube (MCPMT) (Hamamatsu Photonics, Bridgewater, NJ). Each BGO array element measures 2.15×2.15 mm in cross section and is optically isolated from neighboring pixels using a thin reflective film. The crystals vary in height from 7.7 mm to 10 mm in order to achieve a circular profile which allows the front end of

the detector modules to be placed in close proximity to the animal subject. The array elements are open on the front end and act as an optical fiber bundle for channeling bioluminescence SPEs towards the photocathode of the PMT. The MCPMTs have an *extended-red* multialkali photocathode with a quantum efficiency (QE) of 12.4% at 620 nm, compared to 5.3% for the bialkali photocathode version. The multialkali photocathode allows the PMT detector to have a comparable QE for both scintillation (QE = 15.1%) and bioluminescence SPEs.

A custom detector casing was designed and fabricated in order to secure the individual crystals in an array configuration and at the same time optically couple them to the glass surface of the PMT.

C. Analog Electronics

Each of the 64 channels of the MCPMTs has an individual anode readout, resulting in 384 channels for the full ring system. In order to reduce the total number of detector channels, a custom built charge divider network is used, reducing the number of readout channels to four corner channels per MCPMT (24 channels total) [4]. Standard positioning logic (weighting calculation) is used to determine the event position.

A custom built circuit housed in a Nuclear Instrumentation Module (NIM) was used to switch between either PET or SPE mode to filter γ -ray or SPE events, respectively. All signals pass through relays and are sent to either passive low-pass filters (PET mode) or shaping amplifiers (SPE mode). For the PET mode, all signals pass through a low pass filter (-3 dB at 5 MHz). For operation in SPE mode, all signals pass through 24 shaping amplifiers each with a gain of ~ 13 at a shaping time constant of $\tau = 65$ nsec. The SPE shaping time was chosen to match the fast pulse shape of SPEs from the detector module, which includes the response of the MCPMT and readout electronics. All signal channels pass through equal coaxial cable lengths to maintain accurate timing information. The resulting 24 signals are subsequently sent to the DSP unit for event processing.

D. Digital Signal Processing Unit

Recent advances in digital electronics have allowed digitally-based PET systems to take the place of their analog predecessors [5]–[7]. In OPET, analog channels from either the PET low-pass filters or the SPE shaping amplifiers are sent to a DSP unit for event processing. The DSP unit is comprised of three, 8-channel (24 channels total) VHS-ADC (Very High Sampling—Analog to Digital Converter) Virtex-4 boards (VHS boards) (Lyrtech Signal Processing, Quebec City, Quebec). Each VHS board has one 105 MHz Analog-to-Digital Converter (ADC) per input channel on the front end which sends digitized samples to a Virtex-4 Field Programmable Gate Array (FPGA) (Xilinx, San Jose, CA). The three VHS boards are housed in a cPCI chassis. The FPGAs are programmed to process events using either a PET or SPE signal processing algorithm. An external PRL-171 100 MHz clock (Pulse Research Labs, Torrance, CA) acts as the master clock for the VHS boards and also provides a synchronized start signal for the timestamp on each VHS board. Events are processed in real time and data can be communicated between VHS boards via a Rapid Channel (RCH) communication bus. The RCH uses a fixed internal 500 MHz clock and

has a bandwidth of 1 GBps. On each VHS board the RCH has a transfer and receive port, each with eight 8-bit data line pairs of data. Transfer and receive ports between VHS boards are connected using a micro-coaxial cable. Events processed by the FPGA are written to an external Ethernet disk which is connected to the cPCI chassis via a standard Ethernet port.

Signal processing algorithms were developed and tested in the Simulink (The Mathworks, Natick, MA) environment using Xilinx and Lyrtech software tools. These algorithms were automatically converted to generate Very High Speed Integrated Circuit (VHSIC) Hardware Description Language (VHDL) bit-streams which control the functionality of the VHS boards in the DSP unit. The DSP reproduces analog equivalent functions within the digital domain while providing a higher degree of functionality and flexibility resulting in ease of configurability by the user and a reduced need of post-processing of data.

E. PET

1) Coincidence Algorithm—For γ -ray events, determination of event energy, position, and time of arrival are of importance for accurate image reconstruction and quantification. Individual signal processing algorithms were developed which include: energy determination-discrimination, position determination and look-up, digital constant fraction discrimination (dCFD), and coincidence processing. Combining these individual components together provided the PET coincidence algorithm. In the coincidence algorithm each γ -ray singles event is tagged with a 64-bit *event word* within the FPGA which identifies the event: type (*Type ID*, 2-bits), detector (*Detector ID*, 3-bits), position (*Pixel ID*, 6-bits), energy (*Energy*, 12-bits), and timestamp (*Coarse Time—Fine Time*, 41-bits). Fig. 3 shows the bit size for each section of the *event word* used in the FPGA processing and event recording. Singles events from VHS boards 3 and 2 are sent to VHS board 1 for coincidence processing. Within the coincidence processor, the timestamps from incoming single events are compared between all detector pairs (15 total). For valid coincidences the *event word* minus the timestamp is recorded thus, reducing the event information to 23-bits. The VHS recording module records data samples using a fixed write size of 4-bytes per sample.

Both the PET and SPE algorithms record a *time tag* which is inserted into the recorded data stream every 100 msec. The *time tag* has a unique 2-bit Type ID which allows it to be identified in post-processing. The *time tag* provides the overall acquisition time and the ability to gate data sets for reconstructing dynamic activity distributions.

2) Digital Constant Fraction Timing—The dCFD determines the zero-crossing system clock sample by taking the 4-channel sum signal from each detector which it multiplies by a constant fraction, and then adds to the original signal which has been inverted and delayed. The zero-crossing sample provides the *Coarse Time* (36-bits) with a resolution of 10 nsec. A linear interpolation of the positive and negative time points of the *Coarse Time* provides the *Fine Time* (5-bits) with a resolution of 312.5 psec. The *Coarse Time* and *Fine Time* are concatenated providing the event timestamp (41-bits). The constant fraction and delay values were selected to produce the optimal timing resolution between detector pairs.

3) PET Performance—PET performance parameters were measured using different configurations of the coincidence algorithm. The intrinsic spatial resolution was measured

by stepping a ^{22}Na source linearly along the midline of an opposing detector pair while taking coincidence count profiles. To measure the timing resolution, two detectors were placed in coincidence mode and the difference in timestamps between coincidence event pairs was recorded. To determine energy resolution a ^{68}Ge flood source was placed in front of the detectors and energy spectra were measured for each detector element. The absolute sensitivity of a two-detector pair was measured by placing a ^{22}Na point source at the center of the field of view and taking the ratio of energy-qualified coincidences and the known calibrated source activity.

To test the PET coincidence algorithm a phantom with five rods was filled with $10\text{ }\mu\text{Ci}$ of 2- ^{18}F fluoro-2-deoxyglucose (FDG) solution. Each rod measured 0.8 mm in diameter and the corner rods were separated with a center to center distance of 6.3 mm. Coincidence data was collected for two opposing detectors for 5 minutes at angles of 0° , 60° and 120° simulating the full-ring system and providing 1.5×10^6 coincidence events.

Due to the acceptance of coincidence events between all adjacent detector modules in the full ring system, inter-detector scatter and inter-crystal scatter is an issue to be considered. Computation of the system response matrix used in the image reconstruction includes inter-detector scatter and inter-crystal scatter. The full impact of these scattered events has not been evaluated experimentally.

F. Optical

1) SPE Algorithm—The SPE algorithm determines and qualifies the energy and position information for SPE events similarly to that of the PET events without the need for individual event timing information and coincidence processing. The *time tag* value provides the overall acquisition time and gating ability. A digital $5.0\text{ }\mu\text{sec}$ *VETO* is used to discriminate against the BGO *afterglow* which is due to the decay of scintillation SPEs arising from γ -ray interactions. The *VETO* concept and scintillator *afterglow* have previously been described [8], [9]. At a typical expected count rate of the MCPMTs (~ 10000 cps) the SPE mode dead-time due to the *VETO* corresponds to only 5%.

2) Optical Performance—An optical pattern mask was placed on the front end of one of the detector modules. A 600 nm SPE source was placed alongside a positron emitting source ($10\text{ }\mu\text{Ci}$ ^{68}Ge) at a distance of 15 cm from the detector surface providing a flood source of γ -rays and SPEs simultaneously. A 600 nm source was used since the expected bioluminescence signal at the mouse surface will be in the red wavelengths due to scatter and absorption [10]. The SPE algorithm was used to record SPEs and to generate 2D images of the total SPE counts recorded in each detector element.

III. Results

A. PET

PET performance parameters were measured for the two-detector system and are listed in Table I. The intrinsic detector spatial resolution was measured to be 1.49 ± 0.18 mm at the Full Width at Half Maximum (FWHM). The FWHM of the timing spectrum was measured to be 11.8 nsec (Fig. 4). The average pixel energy resolution for the detector pair was 37%.

The absolute sensitivity for the detector pair was measured to be 0.9% for an energy window of 250–650 keV. The parameters measured using digital signal processing are in agreement with those measured previously using analog signal processing for a similar BGO array. One important difference is in the coincidence timing resolution, which is discussed in Section IV.A.

Coincidence data was reconstructed using a 3D Expectation Maximization (EM) reconstruction algorithm. The (a) transverse and (b) coronal views of the reconstructed image are shown in Fig. 5.

B. Optical

Approximately 4.0×10^6 SPE events were collected during a 30 sec acquisition and the resulting 2D projection image was formed. Fig. 6 shows the optical pattern placed on the scintillator array and the resulting raw 2D projection image (with linear color scale). These optical pattern images, while not similar to expected bioluminescence sources, validate the functionality of the SPE DSP algorithm in accurately processing SPE events, as well as the ability to accurately identify the energy and position of SPE events in the presence of a positron emitting source. Thus, the digital *VETO* effectively discriminates against scintillation light, allowing both PET and SPE emitting bioluminescent tracers to be present in the animal subject.

IV. Discussion

A. FPGA Performance

The FPGA based electronics provided functionality comparable to the analog electronics and in many instances, provided several advantages. Positioning logic and pre-defined pixel look-up-tables were implemented in the digital domain, reducing the need for post-processing of the 4 detector readout channels for each event. Similarly, pre-determined energy windows for each detector pixel were employed in the algorithm, allowing for reduced data acquisition sizes. Perhaps the single most important advantage was the ability to process coincidence events in real time, significantly reducing the data size by eliminating the need for recording singles events. A drawback of the DSP was the need for analog filtering and shaping which proved difficult to implement digitally as an Infinite Impulse Response filter.

The results obtained for the two-detector OPET system utilizing DSP electronics provide a validation of the expected PET performance for the full-ring system. The measured intrinsic detector spatial resolution (1.49 mm) agrees with the expected value based on the detector pixel width. The energy resolution (37%) was expected to be broad due to the light loss resulting from the open face of the detector elements. The open-ended BGO crystals act as light guides and channel SPEs from the animal surface to the photocathode of the MCPMT. The digital timing resolution (11.8 nsec FWHM) is comparable to that measured using analog electronics (5.5 nsec FWHM). The 10 nsec sampling resolution of the digital system required an interpolation of the zero-crossing of the dCFD signal, which is thought to contribute to the degradation of the digital timing resolution compared with the analog case.

It is not anticipated that the increase in the coincidence timing window will be important for the typical low activity studies that are to be performed with this tomograph. The digital timing resolution is also in good agreement with the 10.5 nsec digital timing resolution achieved by others using a BGO-Avalanche Photodiode detector pair [11].

B. Full-Ring System

Here, the RCH communication bus was used to transfer PET *event words* between two VHS boards. For the full-ring system the PET algorithm will be expanded to transfer *event words* originating from detectors on VHS 3 and 2 to VHS 1 (Fig. 1). To achieve this, several RCH data interleaving algorithms are currently being tested for their performance.

In its current configuration, OPET has 24 channels to process either PET, or SPE events. Each VHS board can be expanded by adding a daughter board with 8 additional input channels, providing 48 channels total for the three VHS boards. This, along with combining the PET and SPE algorithms into a single dual-modality algorithm provides the ability to record PET and SPE data simultaneously. Similarly, more detector modules could be added to the ring by adding additional VHS boards to the cPCI chassis.

The maximum recording bandwidth of the FPGA based recording module is 20 MB/sec. At 8 bytes per coincidence event this translates into more than one million coincidence pairs per second, which is much higher than the expected PET count rates.

C. Future Work

Previous work utilizing analog electronics has demonstrated that the OPET detector module (scintillator array + MCPMT) has an intrinsic resolution of 2.30 and 2.38 mm FWHM in the transaxial and axial directions, respectively, for SPEs [12]. Additional work includes the implementation of a full-ring PET coincidence algorithm which includes a random coincidences processor. The optical algorithm will be modified to record total SPE counts per detector pixel rather than individual SPEs, reducing the total size of acquisition data. Characterization of the system performance for full-ring PET and optical modes will also be measured. For PET and SPE modes this includes the system dead time. The design of an optical phantom and tomographic reconstruction of a bioluminescence source are also underway [10], [13].

V. Conclusion

A prototype OPET system has been assembled and used to image PET as well as optical sources in the presence of radioactivity using the same detector modules. FPGA signal processing algorithms have been developed which allow on-line processing of PET coincidences and SPEs, greatly reducing the size of the recorded data sets as well as the need for significant post-processing prior to reconstruction.

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References

- [1]. Ray P, Wu AM, Gambhir SS. Optical bioluminescence and positron emission tomography imaging of a novel fusion reporter gene in tumor xenografts of living mice. *Cancer Res.* Mar. 2003 63(no. 6):1160–1165. [PubMed: 12649169]
- [2]. Prout DL, Silverman RW, Chatziioannou AF. Detector concept for OPET—A combined PET and optical imaging system. *IEEE Trans. Nucl. Sci.* Jun.2004 51(no. 3):752–756. [PubMed: 16429601]
- [3]. Rannou FR, Kohli V, Prout DL, Chatzioannou AF. Investigation of OPET performance using GATE, a Geant4-based simulation software. *IEEE Trans. Nucl. Sci.* Oct.2004 51(no. 5):2713–2717. [PubMed: 16429604]
- [4]. Siegel S, Silverman RW, Shao Y, Cherry SR. Simple charge division readouts for imaging scintillator arrays using a multi-channel PMT. *IEEE Trans. Nucl. Sci.* Jun.1996 43(no. 3):1634–1641.
- [5]. Young JW, Moyers JC, Lennox M. FPGA based front-end electronics for a high resolution PET scanner. *IEEE Trans. Nucl. Sci.* Aug.2000 47(no. 4):1676–1680.
- [6]. Streun M, Brandenburg G, Larue H, Simmermann E, Ziemons K, Halling H. A PET system with free running ADCs. *Nucl. Instrum. Methods Phys. Res. A.* 2002; A486:18–21.
- [7]. Junnarkar, SS.; Purschke, ML.; Pratte, J-F.; O'Connor, P.; Fontaine, R. An FPGA-based, 12-channel TDC and digital signal processing module for the RatCAP PET scanner. *Proc. IEEE Nuclear Science Symp. Conf. Rec.*; Feb. 2008; p. 919-923.
- [8]. Prout DL, Silverman RW, Chatziioannou AF. Readout of the optical PET (OPET) detector. *IEEE Trans. Nucl. Sci.* Feb.2005 52(no. 1):28–32. [PubMed: 16429600]
- [9]. Douraghy A, Prout DL, Silverman RW, Chatziioannou AF. Evaluation of Scintillator afterglow for use in a combined optical and PET imaging tomograph. *Nucl. Instrum. Methods Phys. Res. A.* Dec.2006 A569(no. 2):557–562.
- [10]. Alexandrakis G, Rannou FR, Chatziioannou AF. Tomographic bioluminescence imaging by use of a combined optical-PET (OPET) system: A computer simulation feasibility study. *Phys. Med. Biol.* Sep.2005 50(no. 17):4225–4241. [PubMed: 16177541]
- [11]. Leroux, J-D.; Martin, J-P.; Rouleau, D.; Pepin, CM.; Cadorette, J.; Rontaine, R.; Lecomte, R. Time determination of BGO-APD detectors by digital signal processing for Positron emission tomography. *Proc. IEEE Nuclear Science Symp. Conf. Rec.*; Oct. 2003; p. 1723-1727.
- [12]. Vu NT, Silverman RW, Chatziioannou AF. Preliminary performance of optical PET (OPET) detectors for the detection of visible light photons. *Nucl. Instrum. Methods Phys. Res. A.* Dec. 2006 569(no. 2):563–566.
- [13]. Alexandrakis G, Rannou FR, Chatziioannou AF. Effect of optical property estimation accuracy on tomographic bioluminescence imaging: Simulation of a combined optical-PET (OPET) system. *Phys. Med. Biol.* Apr.2006 51(no. 8):2045–2053. [PubMed: 16585844]

Fig. 1.

Proposed signal processing components consist of the detector modules, analog shaping amplifiers and DSP unit containing three electronic boards (VHS 1–3). Each board has eight ADCs on the front end which send digitized samples to an FPGA. PET γ -ray events are processed and identified with an event tag and sent to a coincidence processor. SPE events are processed in a similar manner without coincidence processing. Valid events are written to an external Ethernet disk.

Fig. 2.
Each OPET detector consists of an 8×8 array of BGO scintillators coupled to a R5900-02-M64 MCPMT and readout using a custom multiplex circuit-board.

Fig. 3.

Each event is tagged with a 64-bit *event word* which identifies the event information. The event tags are sent to the coincidence processor where the timestamp is removed prior to recording valid events.

Fig. 4.
The FWHM of the coincidence timing spectrum was measured to be 11.8 nsec.

Fig. 5.
 (a) Transverse and (b) Coronal views of the 5-rod phantom filled with ^{18}F FDG solution and reconstructed using a 3D EM algorithm.

Fig. 6.
 (a) Optical pattern placed on the detector module and (b) Raw 2D projection image of the optical SPE-mode acquisition.

TABLE I

PET PERFORMANCE PARAMETERS FOR THE TWO-DETECTOR SYSTEM USING A DIGITAL SIGNAL PROCESSING SETUP

PARAMETER	MEASURED VALUE
Intrinsic Spatial Resolution	1.49 mm
Timing Resolution (FWHM)	11.8 nsec
Average Energy Resolution	37%
Sensitivity (two-detector)	0.90%