Dual Low Profile Detector Heads for a Restraint Free Small Animal SPECT Imaging System

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***Abstract*--A small animal SPECT system has been developed for acquiring in vivo images of the bio-distribution of radiopharmaceuticals in unrestrained, unanesthetized small animal models. This system uses two dedicated gamma-ray cameras and an infrared based animal position tracking system mounted on a rotational gantry with an infrared transparent mouse burrow in the center. The original implementation of this system had two compact gamma cameras with an active area of 5 cm x 5 cm. Two new gamma camera detector heads with active areas of 10 cm x 20 cm have been built, tested and installed in the SPECT gantry to replace the 5 cm x 5 cm detectors. The new gamma cameras are based on pixellated NaI(Tl) crystal scintillator arrays, coupled to arrays of compact position-sensitive photomultiplier tubes (PSPMT) to achieve high spatial resolution in a compact, low profile device. A novel cost-effective readout is utilized. The two detector heads are based on a 4 x 8 array of Hamamatsu R8520-C12 (1" x 1"; 6X x 6Y anodes) position sensitive photomultiplier tubes. Each PSPMT array is coupled to a pixellated 10 cm x 20 NaI(Tl) scintillator crystal array with individual crystal elements of 2 mm x 2 mm x 15 mm in size and a septum of 0.25 mm between elements. Samples of phantom and animal studies are presented.**

I. INTRODUCTION

We are developing a new methodology for imaging unrestrained, non-anesthetized animals in which the animal position is recorded during image acquisition and the gamma-ray image data is registered to the time-varying animal orientation[1, 2, 3]. The goal of the project is to develop tools and techniques to acquire high-resolution volumetric SPECT images of the head region of an unrestrained mouse and to register the image volumes with previously acquired microCT (50 – 100 micron resolution) data sets. The mouse will be anesthetized during the microCT data acquisition. The microCT images will serve as a reference frame for the SPECT data. An infrared (IR) based tracking system we have developed provides the position and pose of the mouse's head during imaging. Two IR cameras are used in a stereo approach to determine 3D point locations of three markers that have been glued on three locations on the animal's head. The markers are retro-reflective spheres. During acquisition of the SPECT scan, the mouse will be allowed to move freely in an IR transparent cylindrical mouse burrow 3 cm in diameter that is aligned with the center of rotation of the gantry and located 2 cm from the gamma cameras. The gamma camera image acquisition, the IR tracking system and the gantry motion are each controlled by a separate desktop Dell computer. Gamma event data, animal tracking data and gantry position data are all stored on their respective computers time stamped via a common external clock. The data files are later used to reconstruct SPECT images to the small animal reference frame based on a previously obtained microCT of the animal.

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II. DETECTOR HEADS

We have reported before [1] on the development of a SPECT system composed of two prototype SPECT gamma cameras utilizing position sensitive photomultiplier tubes (PSPMTs). The prototype detector heads were based on the Hamamatsu R2487 PSPMT in which the active area of each detector head is 5 cm x 5 cm. The PSPMTs are coupled to NaI(Tl) arrays also obtained from Saint Gobain in which the crystal elements are 1 mm x 1mm x 5mm in size. There is a 0.25 mm septum between each element.

The 5 cm x 5 cm active areas of these initial gamma cameras are too small to image a whole mouse and to accommodate a reasonable amount of animal motion. While the size was sufficient to allow us to test the concept of animal tracking with simple phantoms, it was clear larger detector heads were necessary to facilitate actual mouse imaging. We are reporting here on the successful construction, testing and installation of two new 10 cm x 20 cm detector heads.

A. Electronics

Each detector head is based on a 4 x 8 array of Hamamatsu R8520-00-C12 PSPMTs (1" x 1"; 6X x 6Y anodes), as shown in Fig. 1.

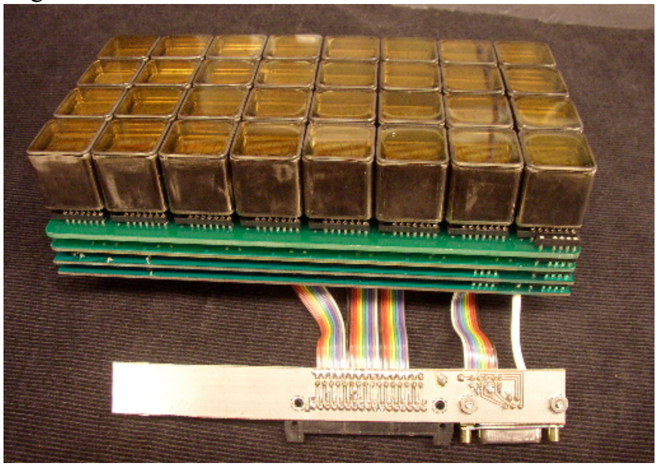

Fig. 1. Photograph of a 4 x 8 array of R8520-C12 PSPMT (1" x 1"; 6X x 6Y anodes) used in each 10 cm x 20 cm detector head.

The readout circuitry for the 32 PSPMTs that make-up the active photodetector area is based on a previously described concept of active subtractive resistive readout electronics [4], but with additional readout channels introduced between individual PSPMTs. In Fig. 2 is shown a schematic of the inter-connection and readout of two of the 32 PSPMTs indicating how the individual strip anode signals are fed via a preamp into a resistive array and how that array is read out.

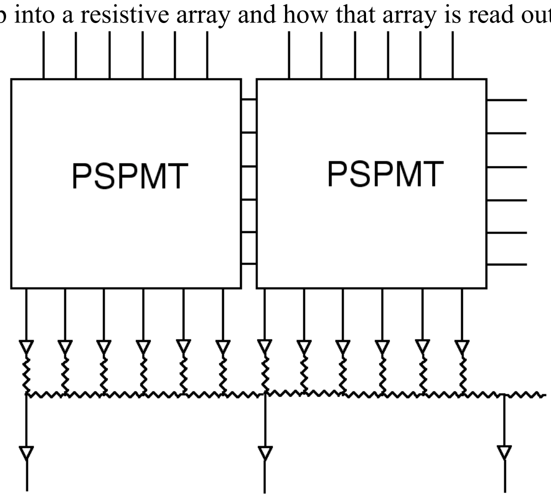

Fig. 2.Schematic of a section of the readout circuit showing two PSPMTs to illustrate the manner in which the signals are picked off at coordinate ends and between PSPMTs

The resistive array consists of a linear chain of resistors on the X and Y coordinates with a total of 24 input channels in the X coordinate and 48 channels in the Y coordinate. The signals from the chain are picked off through another amplifier at the coordinate ends and between each PSPMT row or column to produce 5X and 9Y output readout channels for each detector head.

B. Data Acquisition System

The gamma ray camera data acquisition is controlled by a separate computer from the motion tracking system and gantry motion controller. The data acquisition system for the gamma cameras consists of two 16 channel ADC cards (Datel PCI-416L), a discriminator circuit, a millisecond clock to timestamp the gamma-ray data, and two clocking circuits.

In order to synchronize the data from the gamma camera and the motion tracking system, as well as eliminate data acquired during the gantry motion, a 24-bit clock is read by all of the systems and included in the data. This "system clock" is incremented at 10 millisecond intervals. Since the motion tracking system records an image of the position of the mouse head at 50-100 millisecond intervals, this 10 millisecond update is an appropriate timescale for that motion. It is also sufficient for the gamma ray camera data, as will be describe below.

The gamma camera has an acquisition rate of less than 1 kHz, typically 100-200 Hz. The data from the gamma camera is read directly into buffer memory via a direct memory access (DMA) transfer over the PCI bus. This DMA buffer size is adjusted such that the buffer is filled every 1-2 seconds (i.e. buffer size of 256 events). When the buffer becomes full, it is then transferred to system memory and the data analyzed and plotted in the image or saved to disk memory. The system clock is read every time that the DMA buffer is filled and transferred to system memory. This time is saved with the data from the next buffer and indicates the system time of the first event in that buffer. Since the buffers are transferred every second, the 10 millisecond clock provides ample time resolution to record the transfer of the buffer.

A second timing system is used to record the time of each event within each buffer. This "event time clock" can be set to provide for a 1 msec, 3 msec or 10 msec resolution clock. clock. This "event time clock" is resident in the computer that controls the gamma camera. The clock signal is combined with the gamma ray discriminator circuit and triggers the data acquisition system at the chosen interval. These "timing events" are imbedded within the "gamma events" and saved to memory. The timing events are flagged as timing events so that they can be separated out when the data is analyzed. The time from the "system clock" provides the time of the beginning of the DMA buffer, and a running count of the "event time clock" provides the time of each event within the buffer. The combined time ("system clock" time plus "event time clock" time) provides the time of each event, and is used to synchronize the gamma ray camera data with the motion tracking data. At the low data acquisition rates that were experienced in initial test, the "event time clock" was set to 10.

This Datel PCI computer card is a sixteen channel, 12 bit simultaneous sample-and-hold ADC card with 5 volts input amplitude range [5]. The 16-channel ADC cards and the "system clock" clock are located in a PC that is used to control the gamma camera data acquisition system. The discriminator circuit and "event time clock" are external to the PC. The raw gamma-ray data, the calculated position and energy information, the "system clock" data, and the "event time clock" data are all saved within the event data file for post-processing and analysis with the IR acquired mouse motion data. The KmaxNT development software package from Sparrow Corporation was used to develop software to control the acquisition. This control software generates an image by processing the raw anode data on an event by event basis. This is described in more detail by us elsewhere [6].

C. Scintillator

The 4x8 PSPMT array is coupled to a 10 cm x 20 cm pixellated NaI(Tl) crystal scintillator array with individual crystal elements 2 mm x 2 mm x 15 mm in size and a 0.25 mm septum between each element. The two crystal arrays were obtained from Saint Gobain Crystals and Detectors. Because of the gap between each PSPMT it was not possible to use a scintillator array with the same crystal element step as was used with the prototype NaI(Tl) crystal scintillator arrays with 1 mm size elements.

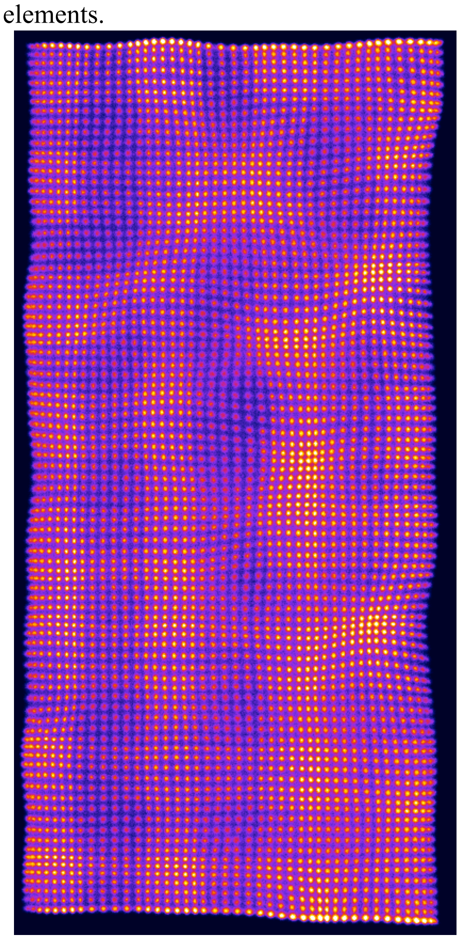

Fig. 3. Raw image formed by flood illumination of a 10 cm x 20 cm NaI(Tl) crystal scintillator array with a ^{22}Na calibration source. The 10 cm x 20 cm pixellated NaI(Tl) crystal scintillator array has individual crystal elements 2 mm x 2 mm x 15 mm in size and a 0.25 mm septum between each element.

We have described elsewhere the calibration process we follow to arrive at the final image for our pixellated scintillator based detectors [7, 8]. Briefly, the calibration of the detector consists of four processes. First, a pedestal measurement is done and then a crystal-to-pixel look-up table is generated via a flood image obtained using a calibration source that emits a high energy gamma such as ^{137}Cs or ^{57}Co. Once the crystal mapping is complete an energy calibration is done for each crystal element using the isotope to be used in the actual imaging in this case ^{99m}Tc99m (or ^{57}Co) and ^{125}I. Finally, flood image is obtained to perform a flood correction.

The data acquisition system treats the output of each crystal element individually to correct for crystal-to-crystal scintillation output variations as well as local PSPMT gain variations. The corrected effective energy resolution of the detector which is obtained from the measured width of the peak for photon energies of ^{57}Co (122 keV) is 19% and 30% from the broad peak from the superposition the photon energies of ^{125}I (27-35 keV).

D. Collimators

The detectors extend axially so that the entire animal can be imaged while in the burrow tube. The detector heads are equipped to accommodate a parallel hole collimator, as well as single pinhole and multipinhole collimators. We have had designed and built several parallel hole and multiple collimators to allow us maximum flexibility in testing our imaging concept. In Table I is a listing of the parallel hole collimators we now have in house to test and use.

TABLE I
COLLIMATORS FOR 10 CM X 20 CM DETECTORS

Image Resolution at 50 mm	Sensitivity cps/mCi	Hole diam (mm)	Septa (mm)	Length (mm)	Material
3.36	7736	1.5	0.19	25	lead cast[A]
3.09	5486	1.2	0.2	23	lead foil[A]
2.45	1717	1.2	0.2	40.5	lead foil[A]
2.13	35	1.2	0.2	69	lead foil[A]
2.68	2056	0.364	0.105	10.6	etched tungsten[B]
3.75	5540	1.397	0.203	27	lead foil[C]
2.70	1602	0.460	0.177	14.3	powdered tungsten[D]

[A] Nuclear Fields USA, Des Plaines, IL
[B] Tecomet, Woburn, MA
[C] Precise Corporation, Caryville, TN
[D] Mikro Systems, Inc., Charlottesville, VA

The detector head housing is constructed of tungsten to shield the 140 keV gamma-ray emissions of 99mTc. Fig. 4 shows a photograph of the 10 cm x 20 cm detector head equipped with a parallel hole collimator.

Fig. 4. Photograph of the 10 cm x 20 cm detector head equipped with a parallel hole collimator.

E. Imaging Results

The 10 cm x 20 cm detector heads are shown in Fig. 5 installed in the SPECT gantry at Oak Ridge National Laboratory. The detector heads have been used in several pilot SPECT animal studies of anesthetized mice. In addition, the new cameras have been used to obtain projection data of moving phantoms to further the development of the mouse tracking system.

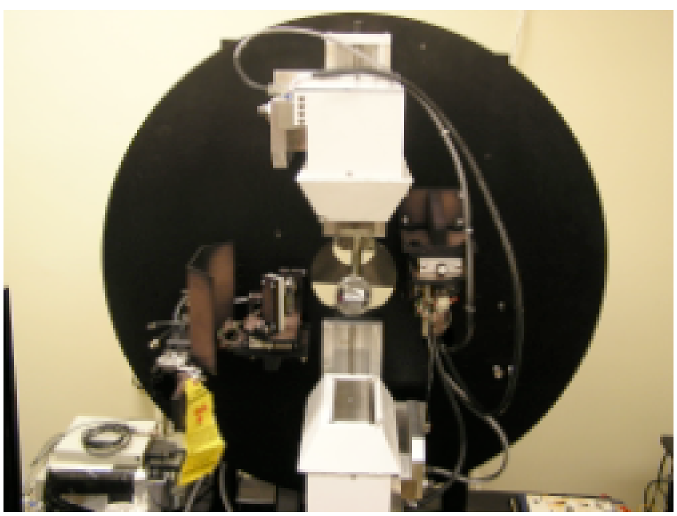

Fig. 5. Two 10 cm x 20 cm detector heads installed in the SPECT gantry shown here with pinhole collimators.

A representative SPECT/CT image is shown in Fig. 6. The specimen is an huIL-6 transgenic mouse model of systemic AA-Amyloidosis imaged with ^{125}I labeled Serum amyloid P component (SAP), which binds with high specificity to amyloid fibrils in the mouse's liver and spleen. The specimen was provided by Dr. Jon Wall of the University of Tennessee Graduate School of Medicine.

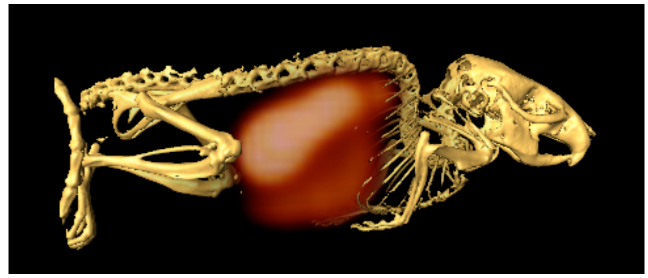

Fig. 6. Merged CT and SPECT image of mouse with systemic amyloidosis affecting the spleen and liver. The specimen was obtained from John Wall at University of Tennessee.

III. Discussion

The complete system: SPECT gantry with two 10 cm x 20 cm detector heads, IR animal tracking system and the separate microCT system are now installed at ORNL (see Fig. 7).

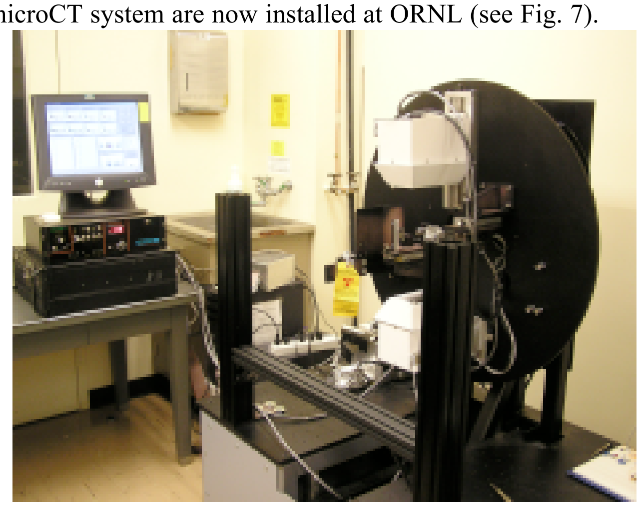

Fig. 7. Photograph of the Oak Ridge National Laboratory imaging system in which the SPECT-IR tracking gantry with two white 10 cm x 20 cm detector heads installed.

The two 10 cm x 20 cm detector heads have been constructed and were successfully used in the SPECT gantry. We have used the SPECT system with a specially constructed three point phantoms to obtain geometric calibration parameters for pinhole and parallel hole collimators which is need to insure high quality high resolution tomographiic reconstruction. The techniques we are using are based on Beque et al [9, 10]. We have just commenced a series of measurements using awake mice with ^{57}Co calibration sources attached to their heads. The studies are being used to validate our list mode based iterative reconstruction algorithms that have already undergone testing with simulated tracking data.

The 10 cm x 20 cm detectors have an intrinsic spatial resolution defined by the 2.25 mm step in the scintillator array. In order to improve this, we are building two new 10 cm x 20 cm which make use of a 10 cm x 20 cm pixellated NaI(Tl) crystal scintillator array with individual crystal elements 1 mm x 1 mm x 5 mm in size and a 0.25 mm septum between each element. The crystal arrays were also obtained from Saint Gobain Crystals and Detectors. In tests with the 10 cm x 20 cm detectors based on the Hamamatsu

R8520-C12 PSPMT it was not possible to resolve the crystal elements which spanned the gaps between the PSPMTs that make up the detector array. We have been able to resolve 1 mm x 1 mm scintillator elements across the gaps of detectors made of combined Hamamatsu 8500 52 mm x 52 mm flat panel PSMPTs [11] and have begun the construction of 10 x 20 cm detector based on a 2 x 4 array of the Hamamatsu 8500 PSPMTs.

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V. REFERENCES

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