Instrumentation Development of a SPECT-CT System to Image Awake Mice *

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I. Introduction

Oak Ridge National Laboratory (ORNL), Thomas Jefferson National Accelerator Facility (JLab) and Johns Hopkins University (JHU) are collaborating on the development of a SPECT-CT system for imaging unanesthetized, unrestrained mice. The use of anesthesia and physical restraint can change the neurological and physiological processes being studied [1]. With our system the position and pose of the head of the unanesthetized mouse is recorded during list mode SPECT image acquisition. The gamma-ray image data is later registered to the time-varying animal orientation. The final system will acquire high-resolution SPECT images of the head region of an unrestrained, unanesthetized mouse and to register the image volumes with microCT data sets of the same mouse acquired separate from the SPECT scan while the animal is anesthetized. We have reported earlier on the development of this small animal SPECT system [2] [3] [4]. See Fig. 1.

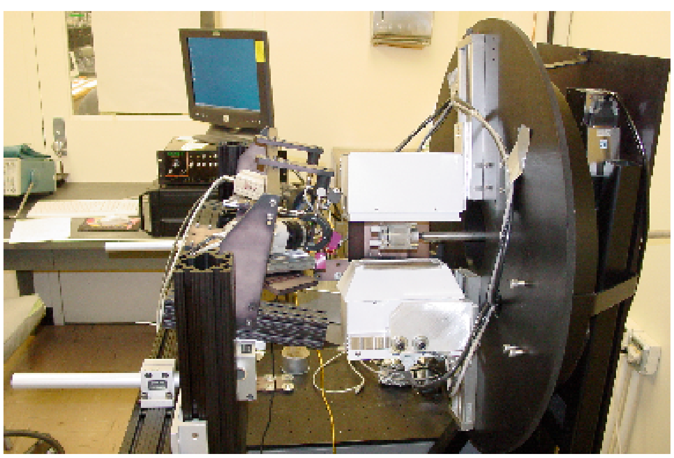

Fig. 1. Photograph of the prototype system at Oak Ridge National Laboratory. Shown is the the SPECT-IR tracking gantry with two white 10 cm x 20 cm detector heads installed. The detector heads are based on a 4 x 8 array of R8520-C12 PSPMT (1" x 1" ; 6X x 6Y anodes).

Three Dell workstations are used to control the three sub-systems (gantry, IR tracking and gamma camera) and record three separated data sets that are later used to reconstruct the SPECT projections. The three data sets that are time tagged via a common clock are: gantry location, mouse pose and gamma camera list mode data. This system uses an infrared based animal position tracking system while acquiring SPECT projections. The awake mouse is confined within an infrared-transparent burrow at the center of rotation of the gantry. The 3 cm diameter burrow is treated with IR anti-reflectance coating to reduce reflections. The mouse will have three infrared reflecting hemispheres attached to its head that are imaged by a pair of CMOS based infrared cameras while illuminated with two sets of IR LEDs. The tracking apparatus will measure the spatial position or pose of the mouse's head with 6 degrees of freedom at a rate of 10-15 frames per second with sub-millimeter accuracy.

A prototype gantry using two gamma cameras with active areas of 10 cm x 20 cm based on an array of position sensitive photomultiplier tubes (PSPMTs) has been constructed and used for phantom tests at Oak Ridge National Laboratory. The gamma cameras are constructed out of a 4 x 8 array of the flangeless compact Hamamatsu R8520-00-C12 PSPMTs (1" x 1"; 6X x 6Y anodes). The array of PSPMTs is optically coupled to a 15 mm thick scintillator matrix with the crystal elements having a 2.25 mm pitch. Several phantom and awake animal tests were conducted at ORNL with the prototype gantry. SPECT reconstruction algorithms have been developed and tested on moving phantoms demonstrating our ability to remove the effects of movement [5].

We have recently installed at Johns Hopkins University a second imaging system using an upgraded SPECT gantry with X-ray CT capability. Additionally, two higher resolution gamma cameras 10 cm x 20 cm in size with finer pitch scintillator arrays are under construction for use on this SPECT gantry in preparation for animal studies. The gamma cameras are based on pixellated NaI(Tl) crystal scintillator arrays and arrays of compact flat panel PSPMTs to enable high spatial resolution in a compact low, profile device.

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II. Methods

The SPECT-CT gantry at Johns Hopkins University is a custom modified Siemens MicroCAT II Small Animal Imaging System. The MicroCAT II is equipped with an 80 kVp (max), 40W x-ray source and a 2048 x 3096-pixel (image resolution 25-50 microns) detector with up to 5-frame per second readout. The gantry includes a three-axis precision motion control system, vibration isolation, a fully interlocked FDA compliant x-ray cabinet, and a removable mouse bed. The system is configured for respiratory gating and outfitted with SPECT mechanical mounts and electronics. It comes with a Dell workstation for implementation.

The gamma cameras for the SPECT-CT imager are based on a 2 x 4 array of the Hamamatsu H8500 flat panel PSPMTs (2” x 2”; 64 PADS). The PADs of a module composed of a 2x2 array of the H8500’s are connected through resistors in rows and columns resulting in a 16 x16 readout for each 2x2 module. Two modules are stacked together resulting in a 20 cm x10 cm detector with a total of 64 channels required for readout. The 64 channels are digitized via two VME 32 channel peak sensing ADCs. Please see Fig. 2.

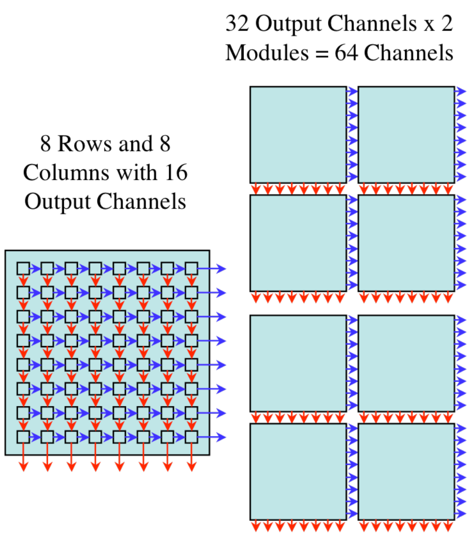

Fig. 2 Schematic diagram showing how the PSPMT signals are combined. On the left is illustrated how the individual PAD signals are connected resulting in a 16 output channels. On the right is shown how the rows and columns of the PSPMTs are connected resulting in 32 channels per 2x2 module.

The data acquisition system is built around a Motorola VME single board computer running the VxWorks [6] real-time kernel. At the front-end the analog channels of the detector are digitized using two CAEN (Model V785) peak sensing ADC modules. All 32 inputs can be simultaneously digitized, buffered, and enabled for a new trigger in less than 6 μsec. Control of the VME CPU and gamma camera image formation is managed by the Java based Kmax [7] data acquisition package running on the PC and communicating to the VME CPU through an ethernet connection. The 10 cm x 20 NaI(Tl) scintillator crystal array has individual crystal elements 1mm x 1mm x 6mm in size and a 0.2 mm septum between each element. See Fig. 2.

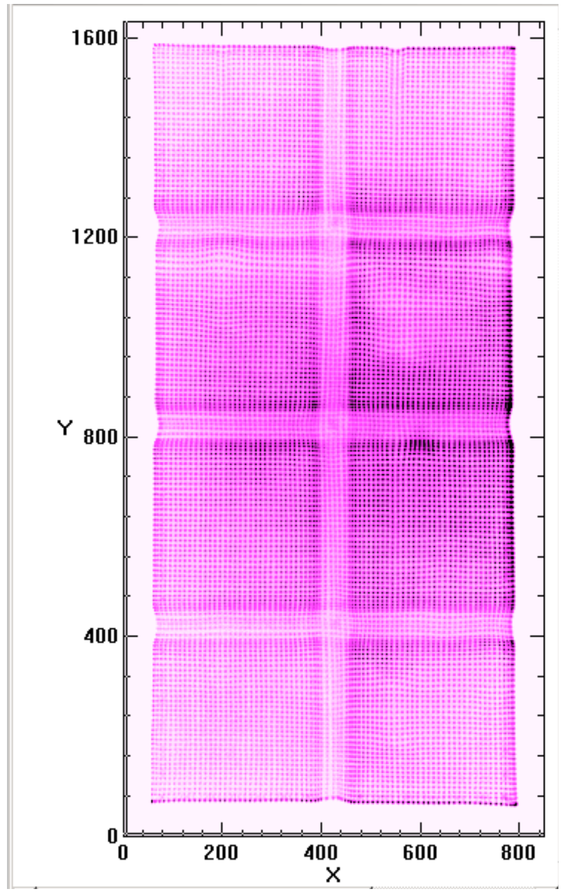

Fig. 3 Raw image formed by flood illumination of a 10 cm x 20 cm NaI(Tl) crystal scintillator array with a ^{22}Na calibration source.

The array was obtained from Saint Gobain. The hermetically sealed 10 cm x 20 NaI(Tl) array with a 2mm glass window is optically coupled to the two PSPMT modules with optical grease. The light sharing across the gap between PSPMTs was sufficient to allow resolving of all the individual crystal elements. Please see Fig. 4.

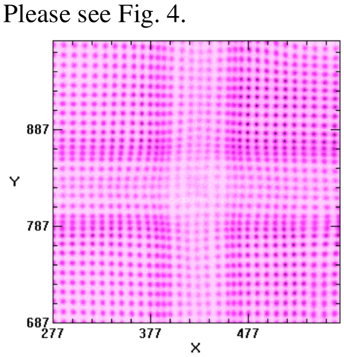

Fig. 4 Enlarged region of Fig. 3 over junction between the top and bottom .

The gamma cameras are designed to image the emissions of ^{125}I and ^{99m}Tc.

An ORNL-JLab optical tracking developmental system is composed of two CMOS optical cameras arranged in stereo configuration, two (sub millisecond strobe) infrared LED array illumination system with the light output aligned coaxial to hemispherical retro-reflective markers by two beam splitters in front of the cameras. The setup provides simultaneous (stereo) blur-free images of the markers. See Fig. 5.

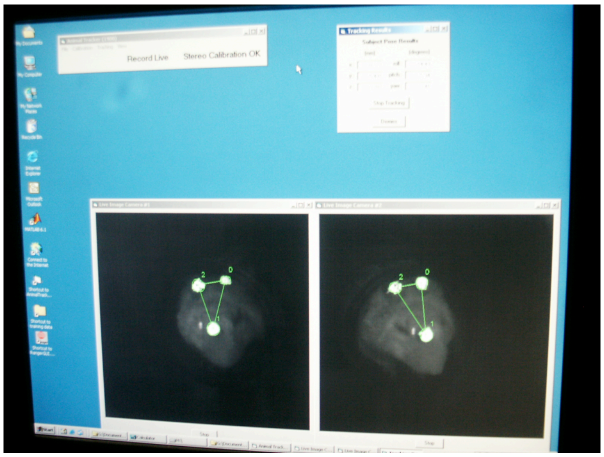

Fig. 5. Photograph of the monitor of the IR tracking Dell workstation control computer showing real-time stereo tracking of markers on mouse's head.

The camera mount assembly is angle and height adjustable to enable sighting slightly down on top of the mouse's head in order to improve the visibility of the markers placed on the upper part of the head. The markers are attached to the animal head using vet bond adhesive applied on their flat side. Dual CMOS camera image acquisition and processing and algorithm development is handled by a Dell workstation. Photograph of the gantry with IR tracking in place is shown in Fig. 6.

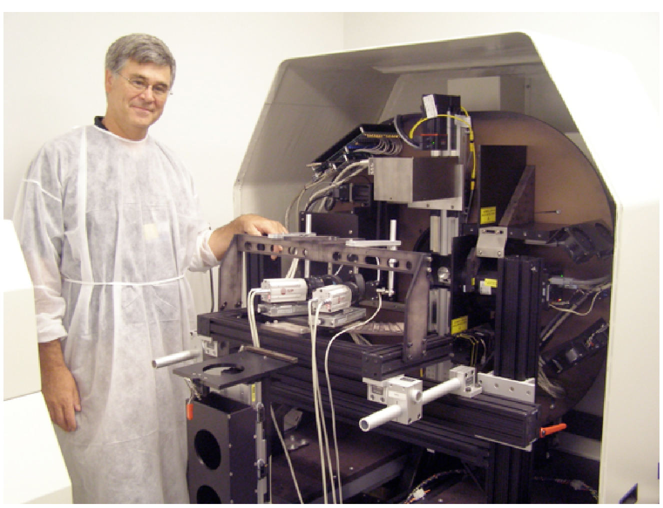

Fig. 4. Siemens MicroCAT II based gantry with the x-ray source and detector and with mounted optical tracking system at JHU. Two CMOS IR cameras are seen in the center of the photograph. A single gamma camera is shown mounted on the sliding stage shown in a vertical position here.

Presently, a single 10 cm x 20 cm gamma camera is in place on the gantry at Johns Hopkins University and awake animal tests have begun. Several awake mice have had there position successfully monitored and recorded with the IR tracking system. We have just recently also acquired several SPECT scans of mice injected with ^{99m}Tc-MDP and we are in the process of reconstructing the images making use of the pose information.

III. Summary

We have in place at Johns Hopkins University a SPECT-CT gantry with the IR optical tracking system installed. The IR tracking system has been tested with several awake mice at Johns Hopkins University. We are in the process of installing two high resolution gamma cameras. One of the cameras is in place and initial animal tests have Our system will be operational in the near future to image pharmocokinetics in the brains of live mice without the confounding effects of anesthesia or physical restraint.

References

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[7]Sparrow Corporation ,1901 Poppy Lane,Port Orange, FL 32128.