SPECT–CT System for Small Animal Imaging

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***Abstract*–The Detector Group at the Thomas Jefferson National Accelerator Facility (Jefferson Lab) and the Biology, Physics and Applied Sciences Departments at the College of William and Mary are collaborating on the development of a miniature dual modality SPECT–CT system for mouse imaging. The detector heads of the SPECT sub-system are capable of imaging the gamma- and x-ray emissions (28-35 keV) of the radioactive isotope iodine-125 (I-125). Two different sets if I-125 imaging detectors are configured on a gantry which has an open-barrel type design. One set of detector heads is based on the 1 inch square Hamamatsu R5900-M64 position sensitive photomultiplier tube coupled to crystal scintillator arrays. The other detector heads configured on the gantry are two 5-inch diameter Hamamatsu R3292-based compact gamma cameras. The x-ray radiographic projections will be obtained using a LIXI Inc. model LF-85-503-OS x-ray imaging system that has an active area of 5.5cm in diameter. The open-barrel shaped gantry facilitates the positioning of various mini gamma-ray imaging detectors and the x-ray system. The data acquisition and gantry control is interfaced through a Macintosh G3 workstation. SPECT reconstruction results using the R5900 based detector are presented.**

I. Introduction

Expanding on our development of imaging detectors optimized for high spatial resolution radiation imaging of the distribution of iodine-125 (I-125) in laboratory animals [1, 2 ,3 4, 5, 6], we report on the design and implementation of an economical miniature SPECT–CT system for mouse imaging. The radioisotope I-125 is readily available commercially as a label for molecular biology probes that are of interest for researchers utilizing small animal research. Others have reported developing systems for I-125 imaging in small animals [7, 8, 9, 10, 11 ,12, 13].

Iodine-125 has a half life of 59.4 days and decays via electron capture with the emission of a ~35 keV gamma-ray followed by the emission of 27-32 keV Kα or Kβ shell x-rays from the daughter product Te-125. The long half-life is an advantage for *in vivo* animal imaging. Though the low energy gamma- and x-rays and long half-life are not suitable for imaging in humans, any tracers labeled with I-125 can also be labeled with I-123 which emits gamma-rays at higher energy (159 keV). Iodine-123 has a much shorter half-life (13.3 hours) which, together with its energy, makes it more suitable for human imaging applications. This adds to the versatility of the use of this isotope.

Others have reported the use of PSPMTs coupled to scintillator arrays to construct high resolution compact gamma cameras [14, 15]. In our application, to image the bio-distribution of ligands labeled with I-125 in the animal under study we anticipate being able to employ two different sets of gamma-ray imaging detectors based on position sensitive photomultiplier tubes coupled to crystal scintillator arrays. One set is based on three 1 inch square Hamamatsu R5900-M64 PSPMTs and the other makes use of two 5 inch diameter Hamamatsu R3292 PSPMTs. The x-ray radiographic projections are obtained using a LIXI Inc. model LF-85-503-OS x-ray imaging system that has an active area of 5.5 cm in diameter. SPECT reconstruction results using the R5900 based detector are presented for two phantom studies.

II. Detector System

The two sets of I-125 imaging detector systems and an x-ray imaging system are configured on a gantry which has an open-barrel type design. The animal bed can be moved to position the mouse at either set of imaging systems. Please see Fig 1.

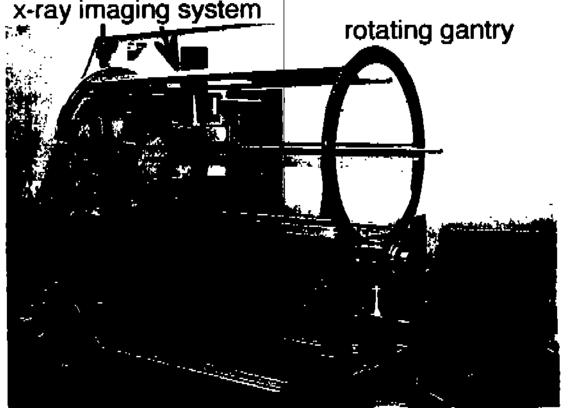

Fig. 1: Photograph of the barrel-gantry. Only the LIXI x-ray system is installed. The animal bed is removed.

A. *Hamamatsu R5900-M64 Based Detectors*

The first set of detectors we are constructing is composed of three detector heads based on the Hamamatsu R5900-M64

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PSPMT coupled to crystal scintillator arrays and utilizing high resolution lead and copper collimators. The three detector heads are installed on mounting plates which can be moved as a unit to accommodate various animal sizes (please see Fig. 2).

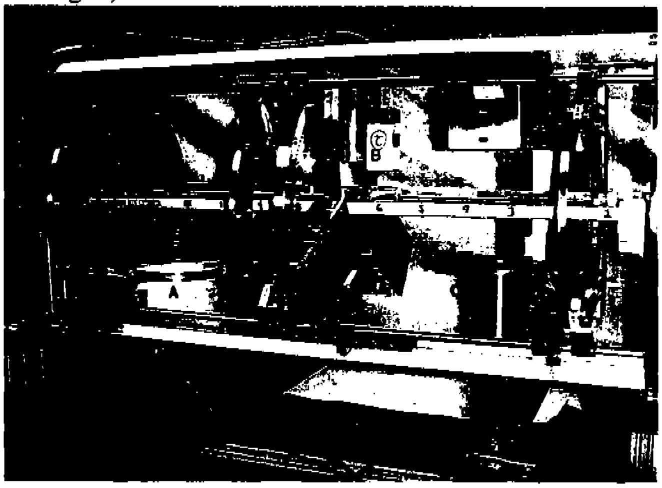

Fig. 2: Photograph of gantry with A) a single R3292 based detector in place, B) a single R5900 detector in place on one of the movable mounting plates and C) the LIXI x-ray imaging system.

Each Hamamatsu R5900-M64 PSPMT has an active area of 18.1 x 18.1 mm^2 and can provide unusually high resolution in imaging. The R5900-M64 is equipped with 64 anode pads which are read out and digitized. We have developed a novel readout circuit to reduce the number of channels that must be digitized from 64 to 16. The readout and amplifier circuitry is contained on a printed circuit board with is attached to each PSPMT. The readout boards accomplish the following two functions: (1) amplify and invert the dynode signal that is later used to produce a trigger to the ADC data acquisition system, (2) de-couple the 64 channel anode pad readout into an 8 X-channel by 8 Y-channel sectorized readout.

A conceptual schematic and the design of the de-coupling circuitry are shown in Fig. 3.

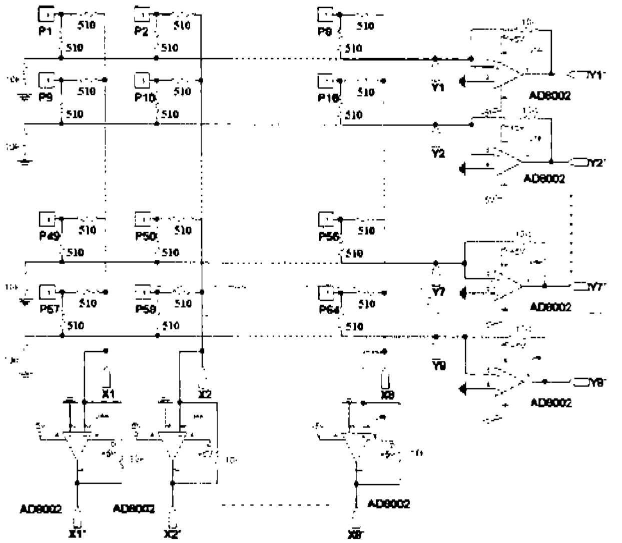

Fig. 3: Array of de-coupling resistors converting the 64 pad anode channel readout into sixteen channel (8x and 8y) strip readout.

The resistor matrix composed of pairs of 510 Ohm resistors, de-couples and combines the 64 individual pad signals into sixteen strip readout channels. The current signal from each anode pad is divided into two equal portions that are collected and amplified by identical low impedance amplifiers. The parameters of the resistor and amplifier network were selected to provide efficient signal coupling and low inter-channel cross-talk. Each of the amplified sixteen strip signals is connected to sixteen channel FERA ADCs from LeCroy (model 4300B). The signal from the dynode of the PSPMT is inverted and amplified before passing through the discriminator electronics so as to detect an event and determine if the signal amplitude is above a desired background and noise threshold, and to generate a 1 μsec wide gate to FERA ADCs. The gate signal to the ADC's is generated by a logic OR of the discriminated dynode signals from the R5900-M64 PSPMTs. A G3 Macintosh workstation as the host computer running control software which was developed using the Kmax data acquisition system from Sparrow Corporation.

B. *Hamamatsu R3292-02 Based Detectors*

Two 5-inch diameter compact gamma-ray imaging detectors based on the Hamamatsu R3292 PSPMT are coupled to arrays of CsI(Tl). The operation and use of these two detector heads in an existing planar I-125 imaging setup is reported by us [5]. In addition we have reported the use of this system in a diabetes research project utilizing mice [6]. The Hamamatsu R3292-02 PSPMT has 28x28 crossed anode wires. The number of individual channels read out was reduced by connecting anode wires in sector groups of two wires such that the number of channels to amplify and digitize is reduced by a factor of two. We have not found a decrease in position resolution by this operation, because lowered granularity of readout was compensated by an improvement in the signal-to-noise ratio[1]. The original 28x+28y anode wire readout was reduced to 14x+14y wire groups. As with the R5900 PSPMTs we make use of the CAMAC FERA based system to digitize the outputs of the R3292-02 PSPMTs.

Each R3292-02 has a CsI(Tl) scintillating crystal array air coupled to is face. Each CsI(Tl) array is composed of 1 mm x 1 mm x 3 mm sized elements separated by a 0.2 mm thick diffuse white reflecting glue which also covers the back side of the array. The CsI(Tl) arrays were manufactured by Hilger, Ltd. [16]. The thickness of the array was chosen to allow for the efficient collection and transmission of the scintillator light to the photocathode. Most of the 35 keV photons of the decay of I-125 get stopped within the first 1 mm of CsI(Tl). It is planned that the two detector heads will be used with various parallel and pinhole collimators depending on the particular needs of the animal study.

C. *LIXI Based X-ray Imaging System*

We have been using a small fluoroscopic x-ray system manufactured by LIXI Inc. (model LF-85-503-OS) to obtain 5 cm diameter images, several of which can readily be combined to provide structural information of the animal under study to co-register with I-125 planar imaging [5, 6]. Originally LIXI Inc. designed this x-ray imaging system for examining small mechanical objects. This device is routinely employed in the physician's office; its size makes it ideal for small animal imaging. Please see Fig. 4 for an x-ray image of the head of a 30 gm mouse using the LIXI Inc. model LF-85-503-OS x-ray imaging system.

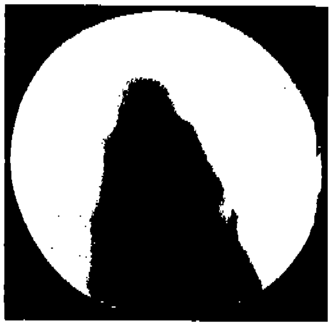

Fig 4. Radiographic image of a mouse's head obtained with the LIXI x-ray system.

The anticipated dose per projection is about 5 rads which is not a significant dose for a mouse. However, we anticipate a total dose of 100 rads (1 Gy) for a single CT scan of 5 cm diameter area of a mouse. The LD 50/30 values for mice range from 7 to 12 Gy for various breeds of mice [17] so a complete body scan may deliver an excessive dose.

D. *Open-Barrel Gantry*

The computer controlled open-barrel shaped gantry facilitates the positioning of the miniature SPECT detector heads or the 5 inch diameter compact gamma cameras and the x-ray system to provide flexible image acquisition. The end rings of the barrel structure are 18 inches in diameter. The gantry is equipped with a motor drive to allow for rotation of the gamma detectors and the x-ray system in order to obtain multiple projections for tomographic image reconstruction. An additional motor is used to translate the animal bed horizontally in and out of the active areas of the gamma detectors and x-ray system. The stepper motor driver is a Velmex, Inc. model NF90 that can control three individual stepper motors. The Velmex driver interfaces to a G3 Macintosh desktop computer via an RS232 port.

II. Preliminary Results

A single R5900-M64 PSPMT was instrumented with a CsI(Tl) scintillator array and installed in the barrel-gantry. Preliminary SPECT reconstruction images were obtained to test the high resolution imaging capability of the system. The I-125 images were generated as we have described elsewhere [4] by determining the center-of-gravity (COG) of the signal from the X and Y anode signals.

Determination of the position of gamma-ray interaction in the scintillator array is determined by computing a truncated center of gravity of the signal distribution on the X and Y anodes of the PSPMT array. This is achieved by using only the digitized signals of those anode wires in the calculation that have a predefined chosen minimal fraction of the sum of all the anode signals (typically 5 to 10%). We have found that the use of this truncated, center-of-gravity (COG) technique is essential to maximizing use of the PSPMT array.

A. *Scintillating Crystal Array Tests*

The crystal scintillating array is a 29 x 29 CsI(Tl) array with crystal element sizes 0.34 mm x 0.34 mm x 2 mm. In this array each element is separated by 0.34 mm white epoxy walls. A flood image of this array is shown in Fig. 5.

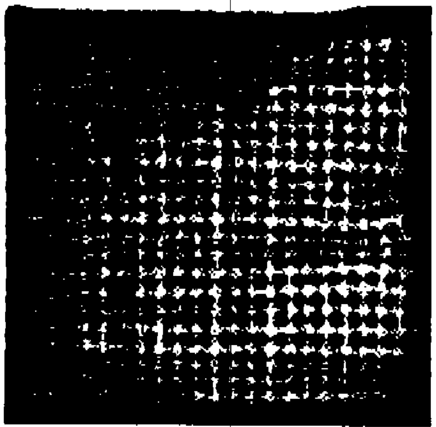

Fig 5. Image of the 29x29 array of CsI(Tl) crystal scintillators flooded with gammas from Co-60 (1.1 and 1.3 Mev). Only the central 24x24 are easily discerned.

The image was obtained by illuminating the face of the detector with gamma-rays (122 and 136 keV) from a Co-57 source. Though nearly each crystal can be identified some distortions exist which are caused by less than ideal selection of de-coupling resistors in the resistor matrix (see Fig. 3).

B. *Planar Image Generation*

The calibration of the detector system to arrive at the final image consists of four calibration processes. First, a pedestal measurement is made and then a crystal-to-pixel map is generated via a flood image obtained using a calibration source which emits a high energy gamma such as Cs-137 or Co-57. Once the crystal mapping is complete an energy calibration is done for each crystal element with I-125. Finally, an I-125 flood image is obtained to perform a flood correction.

As can be seen in Fig. 5, images obtained with PSPMTs exhibit distorted crystal positions because of the non-uniform spatial response of the PSPMT system. Since the relative position of each crystal is known and the crystal locations can be defined in the raw image, a distortion correction is achieved by mapping the data identified to belong to a particular crystal into that crystal's appropriate pixel in a corrected image. From the flood image a look-up table was constructed such that individual crystals are identified by mapping their location from the flood image.

The data acquisition system treats the output of each crystal region individually to correct for crystal-to-crystal scintillation output variations as well as local PSPMT gain variations. For each event the sum of the anode signals is used to generate a pulse height energy spectrum. Using an I-125 source an energy calibration is done for each crystal element. Others and we have reported using this method with arrays of scintillating crystals [18, 19]. Finally a flood image is obtained to perform a final flood correction of the mapped image by using an I-125 flood source.

In Fig. 6 is final image of a ring-channel source phantom filled with I-125. The channel is 2 mm thick and the ring is 1.1 cm in diameter. A 5 mm thick high-resolution lead collimator with 1.22 mm hexagonal cores and 0.15 mm septa was used for this image.

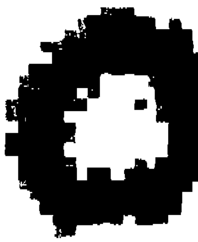

Fig. 6: Image of a ring-channel source phantom filled with I-125. The channel is 2 mm thick and the ring is 1.1 cm in diameter.

C. *High Resolution SPECT*

The small size of these detectors allows the close positioning of three detector heads to achieve the highest SPECT resolution for the rotating heads. To test the high resolution SPECT imaging capability of the R5900 based detector heads we equipped one of heads with a high resolution parallel hole collimator manufactured by Thermo Electron [20].

The copper-beryllium collimator has 0.2 mm x 0.2 mm square openings with 0.05 mm septa and a core thickness of 5 mm. In Fig.7 is a photograph of the collimator.

Fig. 7: Photograph of 5 mm thick copper-beryllium collimator which has 0.2 mm x 0.2 mm square openings and 0.05 mm septa

With this collimator in place, the sensitivity of the detector system was measured to be 110 cpm/μCi. The energy acceptance window was set to 30% below and 50% above the peak emission of I-125 (10 keV - 45 keV).

A phantom was constructed out of five glass capillary tubes. Three tubes were filled with I-125 and a "cold tube" was placed between the three active ones. The inner and outer diameters of each tube are 0.62 mm. and 1.8 mm respectively. A single detector head was used at a distance of 2.5 cm from the center of rotation. A 360° scan was made in which a 3 minute projection acquisition was taken every 3°. The total activity in the phantom is 10 μCi.

A sinogram was generated of the projections and image reconstruction was performed using the iterative maximum likelihood expectation maximization (MLEM) algorithm [21] This algorithm was translated from its original C code into the IDL programming language by Dr. Steve Meikle of the Department of Radiology at the Royal Prince Alfred Hospital in Sydney Australia. In Fig. 8 is an example of an image reconstruction using 30 iterations.

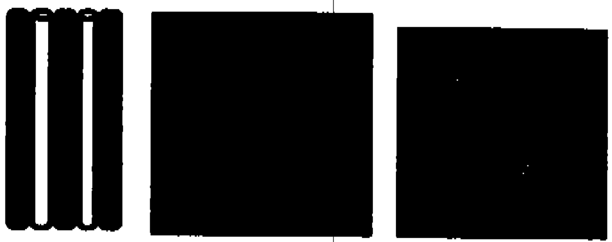

Fig. 8: At the left is a diagram of the capillary tube phantom in which three tubes were filled with I-125 and two cold tubes were placed between them. The centers of the "hot" tubes are separated by 2.7 mm. A projection of the phantom is shown in the middle and a reconstructed slice is shown at the right.

The three hot tubes are easily separated in the reconstruction slice. Another phantom study in which four glass capillary tubes were used. In this test two of the tubes were placed next to each other without a cold tube between them. Please see Fig. 9.

Fig. 9: At the left is a diagram of the capillary tube phantom in which three tubes were filled with I-125 and one cold tube was placed between two of the I-125 filled ones. The centers of the "hot" tubes without the cold tube between them is separated by 1.18 mm of glass. A projection of the phantom is shown in the middle and a reconstructed slice is shown at the right.

In the slice reconstruction shown. the two tubes butted next to each other are almost separated. Though the examples shown here are under ideal conditions in which there is a limited amount of scatter and no background the results nevertheless demonstrate the capabilities of these detectors for high resolution SPECT of I-125.

III. Discussion and Future Plans

We have presented the design and implementation of a barrel type gantry which allows for the installation of multiple imaging systems and permits good access to the animal under study. Our initial results indicate that the combination of the compact Hamamatsu PSPMTs coupled to

CsI(Tl) crystal scintillator will work well as detector heads in a miniature SPECT system.

Ross et al. [22] have reported using an amorphous silicon based flat panel x-ray imager to perform volumetric computed tomography with applications for small animal imaging. We are investigating the use of the LIXI system in a similar fashion. The LIXI x-ray system appears to provide adequate performance for planar acquisition but needs to be further investigated to test its use for the acquisition of CT images of a mouse. The total dose delivered to the mouse may be an issue for a full body scan. At the time we were considering purchasing the LIXI system we were informed by the manufacturer that a version of the system was being developed that delivered with one tenth the dose of the existing model. It was agreed upon that we would purchase the existing model and that within several months we would be able to switch to the lower dose model. However, delays have occurred at the manufacturer and we are still waiting for the model we intended to purchase.

Final construction and detector component testing is underway. We are planning SPECT studies utilizing the 5 inch diameter detectors based on the R3292-02 in which parallel hole and pinhole collimators will be used. In addition we are also investigating the use of NaI(Tl) scintillator arrays. This new scintillator technology was very recently made available to us from Saint-Gobain Crystals and Detectors (formerly Bicron) [23].

IV. Acknowledgment

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