Chapter 18

A Small-Animal SPECT Imaging System Utilizing Position Tracking of Unanesthetized Mice

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1. Introduction

Recent advances in nuclear-medicine based small-animal imaging technology have enabled researchers to acquire *in vivo* images of the biodistribution of radio-labeled molecules in small-animal models such as mice. The standard imaging method requires the use of anesthetic and/or physical restraint to immobilize the mouse during image acquisition of the radioisotope tracer biodistribution. This has the potential to interfere with neurological or other processes that are being studied. With this in mind, Oak Ridge National Laboratory (ORNL) and Thomas Jefferson National Accelerator Facility (Jefferson Lab), in collaboration with Royal Prince Alfred Hospital (RPAH) in Sydney, Australia and Johns Hopkins University, designed and constructed a high-resolution single-photon emission tomography (SPECT) system to study unrestrained, unanesthetized mice. Others have reported development of scintillator based PET isotope probes and systems to study the brain of unanesthetized rodents [Woody, 2001, Zimmer, 2002, Vaska, 2001].

2. Imaging methodology

We have built a SPECT gantry with an infrared (IR) tracking system and a 3-cm diameter cylindrical mouse burrow at the center of rotation (Fig. 18.1). The imaging methodology we have designed digitally records the mouse position and pose during a SPECT scan. The gamma-ray projection data are reconstructed into a fixed small-animal reference frame (SARF) based on the time-varying animal orientation data. The goal of this project is to develop an apparatus to acquire high-resolution volumetric SPECT images of the head region of an unrestrained,

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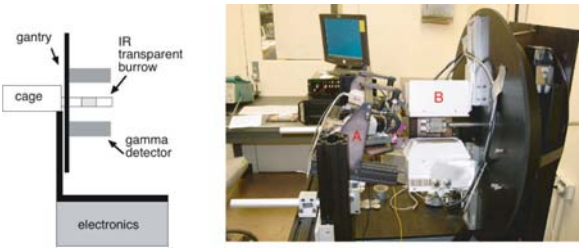

Figure 18.1. Diagram (left) and photograph (right) of the gantry. The IR tracking system (A) and the SPECT cameras (B) are shown in the photograph. The top camera labeled B is shown equipped with a parallel-hole collimator, while the lower camera has a single pinhole collimator.

unanesthetized mouse and to register these image volumes with previously acquired microCT data sets of the same mouse. The animal will be anesthetized during the microCT scan. The microCT images serve as a reference frame for the SPECT data.

An IR-based tracking system developed at ORNL provides the position and pose of the mouse's head during the imaging session. The infrared tracking system is composed of two high-speed CMOS cameras mounted horizontally on a platform facing an IR transparent tubular "burrow" in which the animal is unrestrained during scanning.

The SPECT imaging system is equipped with two 10 cm $\times$ 20 cm detector heads based on an array of position-sensitive photomultiplier tubes (PSPMT). A NaI(Tl) scintillator crystal array is optically coupled to the array of PSPMTs. The system is optimized for iodine-125 imaging, but also is capable of technetium-99m imaging. The use of parallel-hole and multi-pinhole collimation for improved sensitivity with high resolution is being investigated.

Prototype gamma cameras with an active area of 5 cm $\times$ 5 cm, which we have described elsewhere [Weisenberger, 2003], were based on the 3" Hamamatsu R2487 PSPMT coupled to 5 cm $\times$ 5 cm NaI(Tl) scintillator crystal arrays with individual crystal elements 1 mm $\times$ 1 mm $\times$ 5 mm in size with a pitch of 1.25 mm. These cameras were installed in a SPECT gantry at ORNL to perform initial SPECT studies. Time-correlated list-mode data containing the tracking coordinates and the gamma-imaging data acquired from the gamma cameras equipped with a parallel-hole collimator have been obtained of a moving radioactive phantom.

3. Apparatus description

The present apparatus is composed of three subsystems: 1) IR animal tracking system, 2) gamma camera data acquisition system, and 3) gantry control system. Each subsystem is controlled by a separate CPU (Dell desktop PCs). A central clock is read by all three CPUs to generate time-stamped list-mode data so that the projection angle, animal pose, and gamma camera projection data can be used to reconstruct image data in the SARF.

The IR position tracking system was built by ORNL and has been tested with live mice [Goddard, 2002, WebRef]. The IR tracking apparatus is attached to the rotating SPECT gantry. Jefferson Lab has built and installed two 10 cm $\times$ 20 cm compact high-resolution, high-sensitivity gamma-ray imaging detectors for the small-animal SPECT imaging system.

3.1 Infrared animal tracking system

We are developing two different IR tracking methods. The first makes use of extrinsic IR refectors attached to the head of a mouse. The second method uses intrinsic features on the mouse acquired through laser profile tracking. The infrared tracking systems have been described in detail elsewhere [Goddard, 2002, WebRef]. It is composed of two high-speed CMOS IR cameras mounted horizontally on a platform facing a tubular "burrow" in which the animal is unrestrained while being imaged. For the first method, infrared LED arrays and beam splitters are mounted in front of the cameras to coaxially illuminate hemispherical retro-reflective markers placed on the mouse's head. The tracking apparatus is designed to measure the spatial position of the mouse's head at a rate of 10-15 frames per second with submillimeter accuracy.

The tracking system has been tested with live mice such that the position coordinates of mouse's head were successfully tracked. The second method using laser profile tracking (also known as profilimetry [WebRef]) has been tested only with phantoms and is in the initial stages of development.

3.2 SPECT system

Two SPECT gamma camera detector heads are based on a 4 $\times$ 8 array of the Hamamatsu R8520-C12 (1" $\times$ 1"; 6X $\times$ 6Y anodes) PSPMTs. Optically coupled to the array of PSPMTs for each detector head is a NaI(Tl) scintillator crystal array, which has individual crystal elements 2 mm $\times$ 2 mm $\times$ 15 mm in size with a pitch of 2.5 mm. The detectors extend axially so that the entire animal in the burrow can be imaged on the 10 cm wide $\times$ 20 cm long NaI(Tl) scintillator crystal array. The detector heads can be equipped with either parallel-hole or pinhole collimators. We are investigating improving system sensitivity by employing multi-pinhole collimation with image overlap [Smith, 2003, Meikle, 2003]. The detector heads are calibrated and are being tested with SPECT phantoms. Initial phantom studies and modeling studies with multi-pinhole masks have been underway.

The gamma camera data-acquisition system is composed of two 16-channel ADC cards (Datel, Inc., Mansfield, MA), a discriminator circuit, a millisecond clock to time stamp the gamma-ray data, and a 10-millisecond clock used to synchronize the gamma-ray event data with the mouse IR tracking data. A more in-depth description of our data-acquisition system can be found elsewhere [Welch, 2003].

4. Discussion

The overall system concept has been tested with the prototype system in which we have obtained gamma-ray images of a moving phantom source by making use of time-correlated list-mode position tracking data and gamma-ray event data. Preparations for an iodine-125 study are underway to obtain time-correlated list-mode data of a mouse's head position and the gamma-ray event data of an unrestrained, unanesthetized mouse. From the time-correlated tracking and gamma-ray data sets, the iodine-125 uptake in the moving animal's head will be imaged.

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