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Initial Studies Using the RatCAP Conscious Animal PET Tomograph

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Abstract

The RatCAP is a small, head mounted PET tomograph designed to image the brain of a conscious rat without the use of anesthesia. The detector is a complete, high performance 3D tomograph consisting of a 3.8 cm inside-diameter ring containing 12 block detectors, each of which is comprised of a 4x8 array of 2.2x2.2x5 mm^3 LSO crystals read out with a matching APD array and custom ASIC, and has a 1.8 cm axial field of view. Construction of the first working prototype detector has been completed and its performance characteristics have been measured. The results show an intrinsic spatial resolution of 2.1 mm, a time resolution of ~ 14ns FWHM, and a sensitivity of 0.7% at an energy threshold of 150 keV. First preliminary images have been obtained using ^{18}F-FDG and ^{11}C-methamphetamine which show comparable image quality to those obtained from a commercial MicroPET R4 scanner. Initial studies have also been carried out to study stress levels in rats wearing the RatCAP.

PACS:

Keywords: RatCAP, PET, Awake Animal, Conscious Animal

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1. Introduction

Positron Emission Tomography (PET) is a powerful imaging tool that is used for studying functional neurophysiological activity in the brain in both laboratory animals and humans. However, in the case of laboratory animals, except in a few specialized studies [1], it is generally not possible to obtain *in-vivo* images of the brain without the use of anesthesia. This greatly suppresses brain functions and can affect many of the neurological activities that one is trying to study. In addition, one cannot study animal behavior while under anesthesia, which can provide valuable additional information that can be used in conjunction with the functional data obtained with PET

We have developed a small, lightweight portable PET camera known as the RatCAP which can provide brain images of an awake rat. The detector is designed to be mounted to the head of the rat and suspended by a tether which allows reasonable freedom of movement of the animal during the PET scan. We have found that while the detector assembly imposes little physical limitation to the rats movement, a certain level of training is required in order for the anamal to adapt to wearing the camera without undo stress. This paper will describe the detector design and its performance, along with some initial results and PET images that have obtained using the recently completed system.

2. Detector Design

The RatCAP is a small but complete 3D tomograph that is designed to image the brain of an awake rat [2,3]. Figure 1 shows the detector ring prior to installation into its external housing. It has an outer diameter of 72 mm and an inner diameter of 38 mm, and has an axial field of view of 18 mm. The ring contains 12 block detectors, each of which consists of a 4x8 array of 2.3x2.3x5 mm^3 LSO crystals read out with a matching array of avalanche photodiodes (Hamamatsu S8550). The APDs are read out with a custom designed ASIC implemented in 0.18 μm CMOS technology for its small size, high level of integration and low power [4]. This ASIC produces a 32:1 multiplexing of the LSO/APD pixel arrays and delivers a purely digital signal to a readout module that adds a time stamp with resolution of ~ 1.3 ns [5]. The data is then sent in list mode to a separate receiver board, which, in the present design, is based in VME architecture [6]. However, this part of the readout system has recently been redesigned and is being implemented using an optical G-link and PCI based data acquisition system that is more compact and will allow more flexibility in terms of operation. The entire detector weighs less than 200 g and has a power consumption of less than 1 watt.

Fig. 1. The RatCAP tomograph consisting of 12 LSO arrays with APDs and associated readout electronics.

3. Detector Performance

Preliminary measurements have been carried out to determine the initial performance of the detector. The sensitivity was measured to be 0.7% at a threshold of 150 keV and 0.4% at 400 keV. This is somewhat lower than most commercial small animal scanners (e.g., the MicroPET R4, which has a sensitivity of 4.4% at 250 keV), and results mainly from the limited crystal size that can be used in the RatCAP in order to minimize the weight.

Figure 2 shows the radial and tangential spatial resolution as a function of radial distance from the center of the field of view using standard a Filter Back Projection algorithm and a 3D MLEM image reconstruction method. The intrinsic resolution (FPB, no arc correction) is ~ 2.1 mm. The MLEM method gives a resolution of approximately 1.5 mm over the entire FOV, which is comparable to many commercial PET scanners.

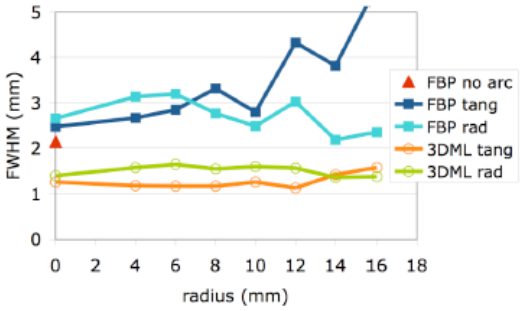

Fig. 2. Radial and tangential spatial resolution as a function of radial distance in the field of view using Filter Back Projection and 3D MLEM reconstruction methods.

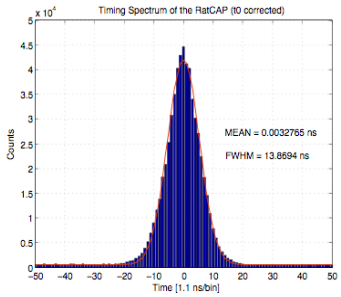

Fig. 3. Coincidence timing distribution obtained by summing many crystal pairs using a ^{68}Ge source in the center of the FOV.

Figure 3 show shows the distribution of time differences obtained from summing over many crystal pairs with a ^{68}Ge point source in the center of the field of view. The distribution has a FWHM of 13.9 ns, which required the use of a 40 ns coincidence time window in our data processing. However, this result was obtained under less than optimal conditions due to some problems that occurred during the initial assembly. The light output variation from pixel to pixel was ~ 6:1, where we expect this to be approximately 2:1. This resulted in an energy threshold that varied from pixel to pixel and required operating at a threshold of 150 keV, which adversely affected the timing resolution. We expect to improve the light output variation in the future, which will allow operating all channels at a higher threshold, and to improve the timing performance of the ASIC in a future design, both of which will improve our timing resolution.

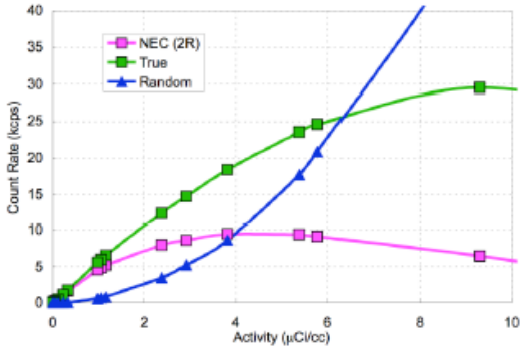

Fig. 4. Counting rates for true coincidences, random coincidences and Noise Equivalent Count rate (NEC) as a function activity concentration.

Figure 4 shows the count rate capability of the RatCAP as a function of activity concentration. Prompt and delayed signals were obtained from the singles data and used to compute the true (T) and random (R) coincidence rates. The Noise Equivalent Count rate (NEC) was computed as $T^2/(T+2R)$. The peak of the NEC occurs at approximately 5 µCi/cc, which is expected to improve significantly when it is possible to make a narrower coincidence time window cut.

4. Animal Studies

The tomograph is attached to the head of the rat using two small posts that are surgically implanted into the skull and held in place with dental cement. A thin inner ring is attached to the posts with small screws, which is then inserted into the main tomograph ring. The entire assembly is supported from above by a tether which is counterbalanced so that the rat does not experience the weight of the ring. Figure 5 shows the tomograph mounted to the head of a rat and supported by the tether.

We have found that rats can easily carry the detector assembly without difficulty, but that they can exhibit high stress levels when wearing the device. Figure 6 shows the corticosterone (CORT) levels in untrained rats wearing the RatCAP. It is clear that the levels remain high while wearing the device compared to the control sample. However, we have also shown that rats can be trained to allow attachment of the inner ring even without anaesthesia,

and that with further training, we expect that they will be able to wear the full detector for 30-60 minutes as would be required for a PET scan.

Fig. 5. Awake rat wearing the RatCAP that is supported by the tether and mechanical counterbalance system.

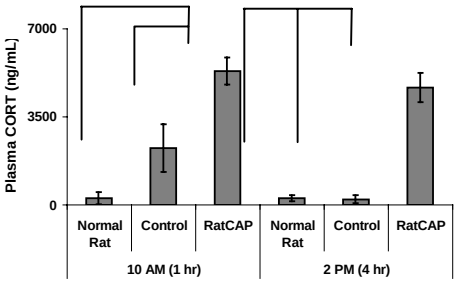

Fig. 6. Corticosterone levels in groups of untrained rats wearing the RatCAP ring compared to a control group having only the RatCAP mounts attached to the head and a normal group that had no intervention.

5. Initial Images

Figure 7 shows some of the first preliminary ^{18}F-FDG brain images of a euthanized rat taken with the RatCAP compared to similar images taken with the MicroPET R4. While the RatCAP has a more limited field of view (as indicated by the white vertical lines in the figure), the quality of the two images is quite comparable.

A second study, shown in Figure 8, was performed to measure the time activity curve for ^{11}C-methamphetamine uptake in a rat brain measured using the RatCAP and compare it with the MicroPET. The results from the RatCAP showed both a regional distribution and temporal dependence that closely resembled that of the MicroPET.

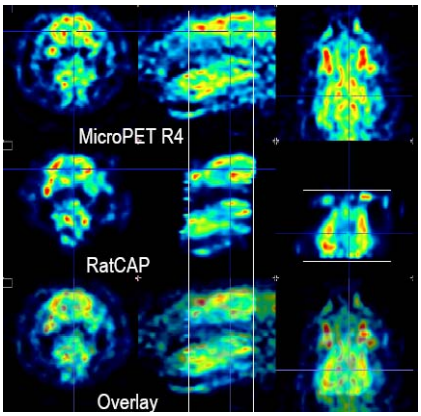

Fig. 7. ^{18}F-FDG rat brain images from the RatCAP compared to the same animal imaged with a MicroPET R4. Vertical lines show the axial coverage of the RatCAP

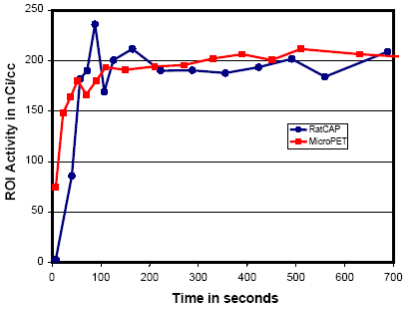

Fig. 8. Time activity curve for a ^{11}C-methamphetamine study using the RatCAP compared to the MicroPET R4.

6. Summary

Initial studies have been carried out with the RatCAP which have shown that the detector is functioning well and shows good performance characteristics. The first images have been obtained and are comparable in quality to those from a commercial scanner. Improvements are expected that will improve the energy and time resolution, image quality, and animal training that will allow better use of the detector for awake animal studies.

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