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Nuclear Instruments and Methods in Physics Research A 527 (2004) 166–170

NUCLEAR INSTRUMENTS & METHODS IN PHYSICS RESEARCH Section A

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RatCAP: a small, head-mounted PET tomograph for imaging the brain of an awake RAT

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Abstract

A small, head-mounted tomograph is being developed which will allow PET imaging of the brain of an awake rat. This device will permit neurophysiological studies to be carried out on small animals without the use of anaesthesia, which severely suppresses brain functions and behavior. The tomograph consists of a 4 cm diameter ring consisting of 12 blocks of LSO crystals, each containing a 4×8 matrix of $2 \times 2\,mm^2$ pixels read out with a Hamamatsu S8550 avalanche photodiode array. The ring will be mounted to the head of the rat and supported by a tether that carries the weight and provides a pathway for electrical signals. Combined with additional mechanical components, it will allow nearly complete freedom of movement of the animal. In order to minimize the weight of the ring, and to keep all of the front end readout electronics as close as possible to the detector, a new ASIC is being developed in 0.18 μm CMOS technology that will process the analog signals and provide digital readout of the pixel arrays and timing information.

This paper will describe the novel features and challenges of this new detector, along with preliminary results obtained with a pair of block detectors used in a configuration similar to the final tomograph. Results are given on studies carried out to optimize the light output of the crystal arrays, measurements of the APDs, a preliminary design of the readout electronics chip, and reconstructed images of various types of phantoms in order to demonstrate the feasibility of the detector concept.

PACS: 87.57.−s; 87.58.Fg

Keywords: RatCAP; PET; Small animal; Tomograph; Brain imaging

1. Introduction

PET imaging has become an increasingly important part of the study of the neuro-physiological behavior of small animals, allowing measurements of physiology, chemistry, and metabolic activity in vivo, which provides information that is ultimately useful for studying similar effects in humans. However, for small animals, these studies presently can only be carried out with the use of anesthesia, which eliminates the possibility of

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doi:10.1016/j.nima.2004.03.114

behavioral studies, and severely depresses brain functions.

One approach to circumvent this problem is to attach a small, high resolution tomograph directly to the head of an awake animal that can provide imaging data, while at the same time allow reasonable freedom of movement. The Rat Conscious Animal PET, or RatCAP, utilizes this approach to image the brain of a live, awake rat. It consists of a single small tomograph ring made up of 12 gamma ray detector blocks along with their associated readout electronics. The design minimizes the weight of the detector and allows the ring to be mounted on the head of the rat, suspended from above, and permitting nearly free movement of the animal.

A feasibility study for this device has been reported previously [1]. This paper describes the concept and design of the tomograph, along with preliminary studies that have been carried out to evaluate its actual performance. Considerable effort is now under way to finalize the design of the detector and readout electronics, as well as studies with live animals to evaluate their behavior when using the device.

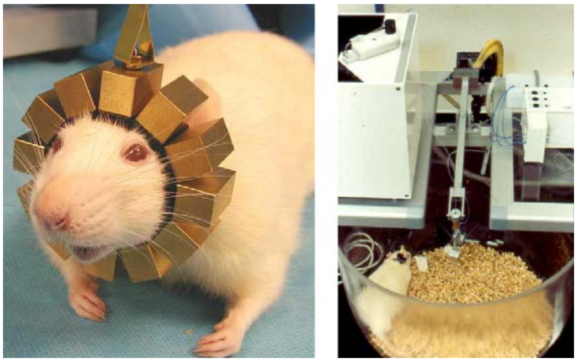

Fig. 1. (a) Mockup of the RatCAP ring on the head of a rat. (b) Ratturn bowl used to support ring and allow freedom of movement.

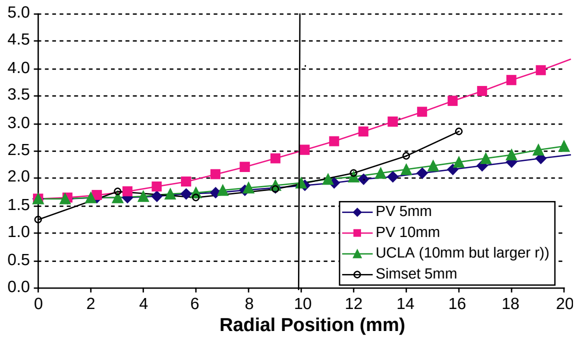

Fig. 2. Position resolution of the RatCAP for 5 (triangles) and 10 mm (squares) thick crystals. Open circles are for SimSET with 5 mm crystals. A comparison is also shown for the UCLA MicroPET. (upward triangles).

2. Detector design

The main design requirements for the detector are to minimize its weight and provide high resolution image data within a very small field of view. The detector consists of an approximately 4 cm diameter tomograph ring containing 12 individual detector blocks. Each block consists of a 4×8 array of $2 \times 2\,\text{mm}^2$ LSO crystals read out with matching arrays of avalanche photodiodes (APDs) and highly integrated custom readout chips.

Fig. 1 shows a mockup of the device on the head of a rat. The total weight of the ring is $\sim$150 g, which is supported from a tether. The animal is free to move in a bowl that follows its movements and keeps the ring suspended over its head. This device, know as a "Ratturn Bowl" is used in microdialysis experiments for a similar purpose.

2.1. Spatial resolution

Due to the small field of view, and the fact that the rat brain nearly fills this field of view, parallax error is a major concern. This error is a function of the depth of interaction of the gamma ray in the crystals, which, in the present design, is determined by the thickness of the crystals. The resolution has been estimated for 5 and 10 mm thick crystals using a simple analytical calculation, as well as for 5 mm thickness using the SimSET Monte Carlo program [2]. The results are shown in Fig. 2.

The initial detector will consist of a single layer of 5 mm thick crystals and will provide a resolution of $\sim$1.9 mm out to a radius of $\sim$1 cm corresponding to the edge of the rat brain. For

10 mm crystals, which would improve the sensitivity of the detector, the resolution worsens to ~2.5 mm. However, this can be improved by using two layers of 5 mm crystals, each with its own separate readout, and is foreseen to be implemented in a future version of the detector. Additional ways of improving the resolution can be found in Ref. [3].

2.2. Light output and energy resolution

A systematic study was carried out to investigate the light output and resolution of the crystal arrays. Crystals arrays were obtained from CTI (Knoxville,TN) and Proteus (Chagrin Falls, OH), each consisting of $2 \times 2\,\mathrm{mm}^2$ LSO crystals of various lengths. The CTI arrays contained a white powder reflector between each pixel, while the Proteus arrays utilized a dielectric reflector manufactured by 3M. Proteus provided two types of arrays, one in which the reflector was glued to the crystals, and a second version which had no optical coupling between the crystals and reflector.

The crystals are read out using a Hamamatsu APD array (S8550) that is designed to match each element in the APD to an individual pixel in the crystal array. Fig. 3. shows the Proteus crystal array and APD.

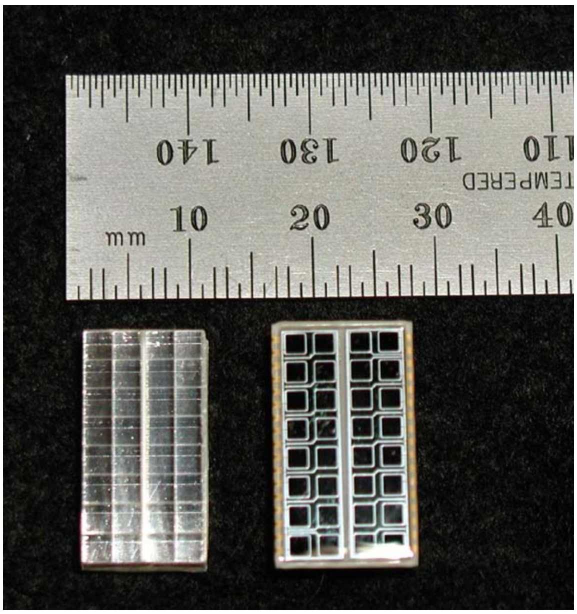

Fig. 3. Proteus crystal array and Hammatsu S8550 APD.

Table 1
Summary of photoelectron yields and resolutions for various crystal arrays measured with Hamamatsu APD array. Resolutions are FWHM for 511 keV gamma rays

Manufacturer	Length (mm)	Type	Npe/MeV	Resolution
CTI	8	Slotted	2370	0.24
Proteus	5	Glued	1577	0.20
	10	Glued	2272	0.19
Proteus	5	Not glued	2506	0.18
	10	Not glued	2914	0.17

The light output and energy resolution of each crystal array was measured with the Hamamatsu APD array using 511 keV gamma rays, and the results are summarized in Table 1.

The highest light output and best energy resolution was provided by the Proteus arrays with no glue between the crystals and reflector. For the 5 mm arrays we plan to use, the light output was ~2500 photoelectrons per MeV and gave a resolution of 18% fwhm.

2.3. Readout electronics

The APD signals will be processed with a custom designed ASIC that will contain a preamp, shaping amplifier and zero-crossing discriminator, along with a serial encoder that will provide a digital address of each pixel that exceeds a given discriminator level that can be set individually for each channel. The leading edge of the serial data will also provide timing information that will be used later to form a coincidence between different detector blocks. The design is implemented in 0.18 μm CMOS technology in order to minimize the power consumption and size of the chip. With this design, the final size of the ASIC will be $\sim 4.3 \times 1.6\,\mathrm{mm}$ and will have a total power consumption of ~125 mW.

The ASICs will be mounted on small circuit boards on the back of the APDs on each detector block. A flexible cable will connect each block together on the ring and serve as a serial bus for transmitting the data and receiving power and

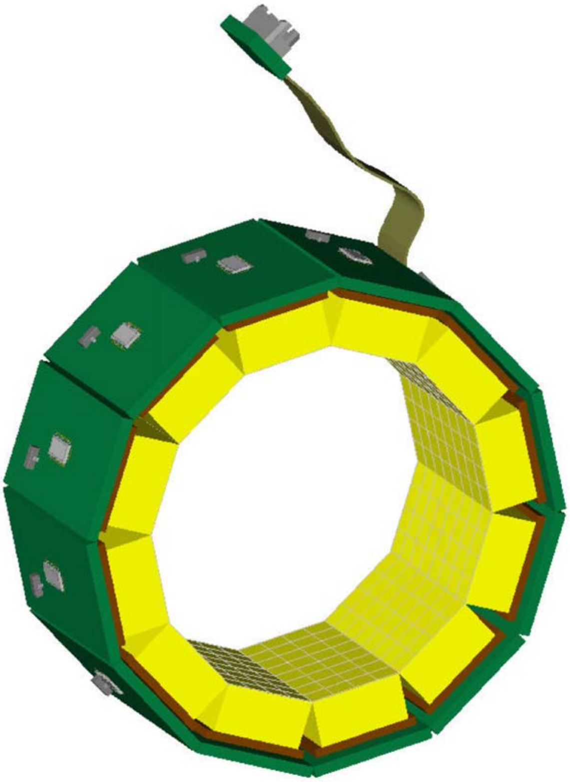

Fig. 4. Block detectors form a ring connected with a flexible cable that serves as bus for transmitting serial data of the ring and receiving power and control signals.

control signals. A conceptual design of this configuration is shown in Fig. 4.

The data containing the address of each pixel that is hit along with its timing information will be sent in list mode via a serial bus to a data collection module located off the ring. The module will collect and time stamp the data, and contain a coincidence processor that will form the coincidence between detector blocks. It will also be possible to collect data in singles mode for calibration and background studies.

3. Preliminary results

A test setup has been constructed consisting of two detector blocks, each containing a 4×8 array of crystals read out with APDs. Since the custom ASIC is not yet available, the APDs were read out with hybrid preamp and shaping amplifiers using a FERA ADC CAMAC system. Data was obtained by rotating these two detectors around various source phantoms in order to study the spatial resolution of the system. Data was collected and binned in sinograms and reconstructed using a filter back projection algorithm.

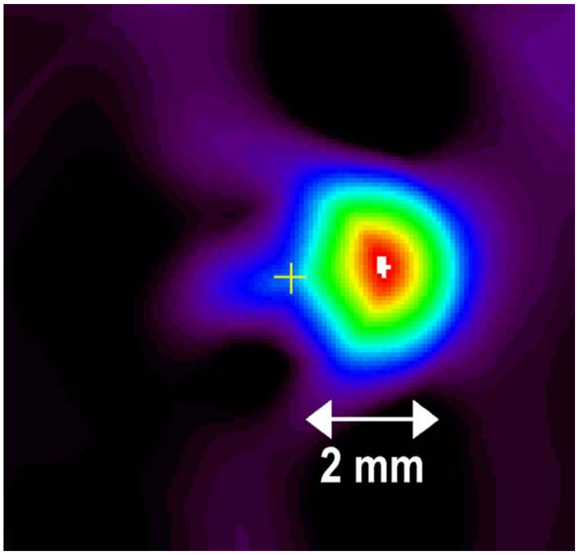

Fig. 5. Point source image taken with a test setup for the RatCAP. The measured position resolution is ~2.1 mm.

Fig. 5 shows an example of a point source image obtained with this test setup. The measured resolution is 2.1 mm, in good agreement with the expectation from simulations.

4. Summary and conclusions

The RatCAP will provide high resolution tomographic images of an awake rat with reasonable freedom of movement. The design of this device is nearly complete, and preliminary tests have shown that the design will meet the requirements for providing the necessary spatial resolution that is required. Efforts are currently under way to construct the first working detector, which should open up many new possibilities for research in neuroscience.

Acknowledgements

This work is supported under a grant from the DOE Office of Biological and Environmental Research and DOE Contract DE-AC02-98CH10886

References

[1] P. Vaska, D.J. Schlyer, C.L. Woody, S.P. Stoll, V. Radeka, N. Volkow, Imaging the unanesthetized rat brain with PET: a feasibility study, 2001 IEEE NSS/MIC Conference Record, Vol. M9A-8, 2001.
[2] S. Kaplan, R.L. Harrison, S.D. Vannoy, IEEE Trans. Nucl. Sci. NS-5 (1998) 3064.
[3] P. Vaska, S.P. Stoll, C.L. Woody, D.J. Schlyer, S. Shokouhi, IEEE Trans. Nucl. Sci. NS-50 (2003) 362.