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## A LSO Beta Microprobe for Measuring Input Functions for Quantitative Small Animal PET

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### Abstract

A miniature scintillation microprobe has been developed to measure the input function in live rodents for use in longitudinal, quantitative PET studies. The probe consists of a small lutetium oxyorthosilicate (LSO) crystal measuring typically 0.3-0.5 mm diameter x 0.5-2 mm in length that is used to directly detect positrons in the blood or tissue. The probe has a sensitivity of 10-30 Hz/ $\mu$ Ci/cc and is primarily sensitive to short range positrons emitted by labeled radiotracers in the blood. The sensitivity to gamma-ray background can be minimized using a variable threshold in the readout to discriminate between positrons and gammas. The probe was implanted in one of the tail veins of a Sprague-Dawley rat and the input function was measured for the injection of 0.8 mCi of FDG in the other tail vein. The probe exhibits a fast time response that is able to quickly and accurately measure the concentration of <sup>18</sup>F circulating in the bloodstream. Additional tests were also carried out to study the probe's sensitivity to gamma ray background.

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## 1. Introduction

Modern biomedical imaging techniques involving small laboratory animals are possible with several high-resolution tomograph devices like micro-PET, micro-MRI etc. These devices give us a better understanding of neurodegenerative diseases and also help us understand the behavioral processes in the animal, thus, help develop better imaging tools. However, the administration of anaesthesia would suppress significant biological measurements and high cost would add to its limitation. Also, the images obtained from these devices are reconstructed images that require the usage of complicated mathematical algorithms leading to poor spatial resolution. Hence, there is a need for more easily administered studies involving the local uptake of radioactivity in awake, freely moving rodents.

A beta microprobe has been designed to measure the radiotracer uptake in the region of interest, which can provide better spatial resolution than PET images, as well as good sensitivity. It directly measures the positron decay activity from radiotracers and has numerous potential applications including the evaluation of new radiotracers in live awake, freely moving rodents. It is similar in size and function to the standard microdialysis probe, but has the ability to measure positrons in a very small volume surrounding the probe. It also provides an ideal method to measure the time versus activity curve in the blood as a function of time (input function) in small animals, which in turn will allow physiological modeling, with an accuracy that has not yet been possible with PET.

## 2. Theory

Beta particles within biological tissue have a short range and will be stopped in a small distance. The principle of the beta microprobe in the detection of these particles relies on the limited range of the particles in the tissue. The probe is carefully placed where beta particles are emitted within the maximum range in the tissue. This proximity is termed as the detection volume of the probe, where positron decay

activity can be measured. It is also possible that the 511 KeV gamma rays, generated due to the annihilation of positrons with electrons can interact with the probe and add to measured betas. In order to differentiate betas from gammas, it is very important to find the detection volume, where the probe is more sensitive to betas.

## 3. Probe Construction

The microprobe consisted of a LSO scintillating crystal of optimum size with diameters ranging from 0.3 to 0.5 mm and lengths from 0.5 to 2 mm. The crystal is carefully mounted onto the tip of the optical fiber having diameters from 0.4 to 0.6 mm for small and large diameter crystals, respectively. Care has been taken with regard to flat polishing of both the crystal and fiber end surfaces before they were glued. Each crystal is glued to the fiber using a fast curing epoxy. The measured optical transmission of the epoxy was 86 % at the 420 nm emission wavelength of LSO. The jacket of the optical fiber is stripped to allow the fiber to pass through an 18-gauge needle, and to be inserted into the blood vessel of the animal.

Once the crystal is glued to the fiber, a thin layer of white reflective coating is applied around the crystal so as to increase the light collection efficiency. A subsequent layer of black latex paint is applied over the white coat, to reduce the sensitivity to room light. In addition, a single layer of polyester shrink tubing (0.034" thickness) was placed over the coated crystal in order to encapsulate the probe tip and protect it from coming in contact with blood or tissue. Smaller probes were constructed in a similar manner, which can be easily mounted inside an 18-gauge syringe needle. All the probes constructed were sufficiently small that they can be easily inserted into a vein or an artery of the animal and can be used to measure the radiotracer activity in the blood. This construction would minimize the physiological effect on the animal.

#### 4. Light Output Measurements

The test setup was comprised of a dark box where the probe tip is pointed towards a strong highly collimated  $^{90}\text{Sr}$  source (10 mCi) to produce < 1 mm diameter beam of up to 2.2 Mev electrons. A low noise photomultiplier tube (Hamamatsu R647P) is used to convert the light produced by the crystal into an electronic signal. The phototube is very quiet and is capable of detecting single photons. The gain of the phototube is calibrated in terms of number of ADC channels per photoelectron. The average photoelectron yield for each scintillation event in the crystal was determined. In order to discriminate the background gamma rays and to obtain a beta measurement without any contamination, the probe is exposed to pure betas from a  $^{90}\text{Sr}$  source and is compared with gammas from a  $^{137}\text{Cs}$  source. From Fig. 1, it is clear that the LSO probe showed a clear separation of betas from gammas.

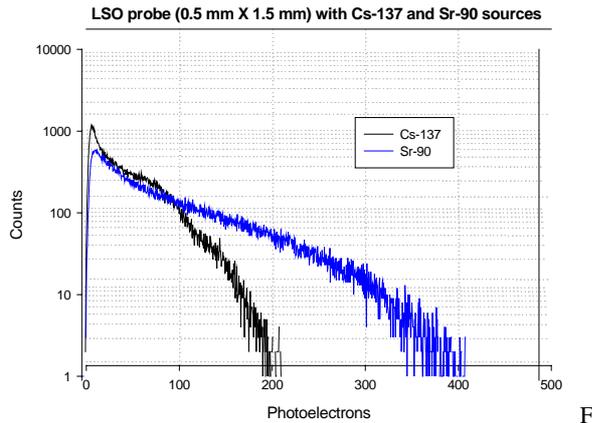


fig.1. Discrimination of gammas from betas.

##### 4.1. Sensitivity measurements

The overall sensitivity of each probe depends on the size of the probe, the amount of energy deposited on

Probes	Dimensions (diameter x length)	Activity ( $\mu\text{Ci/cc}$ )	Count rate (Hz)	Probe Volume ( $\text{mm}^3$ )	Sensitivity ( $\text{Hz}/\mu\text{Ci/cc}$ )
LSO # 15	0.46 mm x 2 mm	274	4280	0.33	15.6
LSO # 16	0.46 mm x 1.5 mm	230	2102	0.25	9.1
LSO # 17	0.55 mm x 2 mm	147	4294	0.47	29.2
LSO # 18	0.5 mm x 1.5 mm	124	1639	0.29	13.2

Table 1. Sensitivity measurements for LSO probes.

the probe material and the efficiency detecting the scintillation light that is produced. The detection efficiency is a function of the number of photoelectrons produced and the threshold set in the electronics for detecting the signal. The relative sensitivity of the probe to positrons and gammas can be achieved by varying the threshold.

The sensitivities of the LSO probes were measured using an aqueous solution containing F-18 with a known concentration of  $315 \mu\text{Ci/cc}$ . The phototube output was sent to a discriminator in order to detect signals above a certain threshold. The detection threshold was set to 50 mV, which was about 20 mV above the pmt single photoelectron noise signal ( $\sim 30$  mV). The measured sensitivities are given in Table I.

Threshold scans were performed on all LSO probes to check the response of the probe at varying threshold voltages during the sensitivity measurements.

#### 5. Result from animal study

The LSO probe of 0.5 mm diameter x 1.5 mm long crystal was used to measure the time-activity curve in the tail-vein of a Sprague-Dawley rat weighing 350g. Before the experiment, the probe was tested for light output detection sensitivity. The count rate due to random background was measured with the room lights turned off and with the probe covered with opaque aluminium foil.

The rat was anesthetized and placed on a bench in a comfortable position. The polyester shrink tubing on the LSO probe is removed for the experiment in order to accommodate the 18-gauge needle that is inserted into a tail vein. An activity of 0.838 mCi in 0.8 cubic centimeter volume was injected into another tail vein of the rat (lower than the LSO probe). The input function is measured for the next 10 minutes. The

count rate peaked at approximately 776 Hz, 30 seconds after the time of injection and then dropped steadily, as shown in Figure 2.

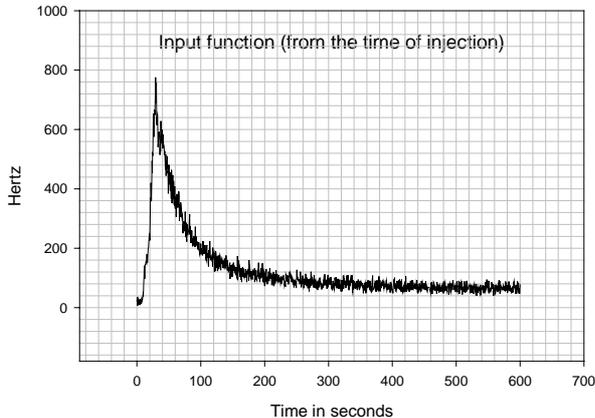


Fig.2. Time-activity curve measured by the probe in the rat tail-vein.

## 6. Sensitivity to Gamma Ray Background

A simulation of the rat experiment was done to study the contribution of gammas to the measured signal with the probe. Radioactive counts were measured using an aqueous solution containing F-18 with a known concentration of 2 mCi in 40 cc volume. The setup replicates the anatomy of two tail veins of the rat using polythene tubes of same dimensions (ID = 2 mm, OD = 4 mm, wall thickness = 1 mm), placed next to each other. The activity was pumped into one of the tubes signifying one of the tail veins of the rat, while the beta microprobe that was used for rat experiment is placed in another tube and counts were recorded from read-out electronics. The tube containing activity was flushed out and the activity was then introduced in the same tube where the probe is placed. Data were recorded and are plotted against time as shown in Fig. 3. From this measurement, it is determined that the contribution from the gamma ray background was only 12.6%.

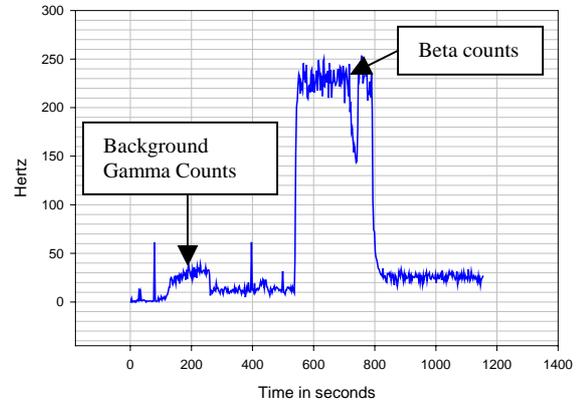


Fig.3. Simulation plot to measure gamma ray contribution in LSO probe.

## 7. Conclusion

A beta microprobe consisting of a small LSO crystal coupled with an optical fibre has given encouraging results to measure the input function of a live rat. Excellent stopping power, high light output, fast response and high detection efficiency characteristics of LSO has made the probe highly sensitive to positrons, offering good discrimination from the background gammas. The sensitivity measurements were carried out to measure the response and detection efficiency of the probes. The high count rate obtained from the input function is reflective of its application to detect the activity in the blood as it passes through the blood vessel.

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