



biospace lab
 β microprobe
Application Notes

Blood input function measurements with the β -Microprobe

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Goal:

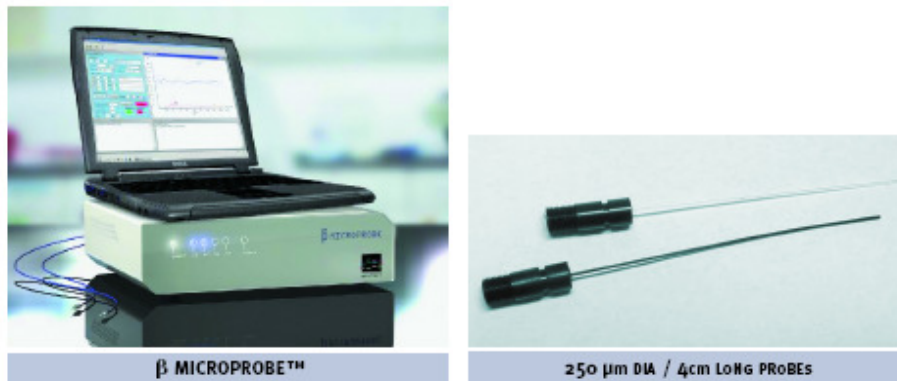
Many important studies in live animals require intravenous injection of a radioactive tracer. To extract relevant biochemical information, time vs. tracer activity curves in physiological regions of interest are developed on the basis of compartmental models that describe the biochemical pathways of the tracer from blood to biological target. These models involve time vs. activity curves in plasma - also called “input function”- that describe the availability of the tracer to the regions of interest.

Usually the input function is measured by repeated blood sampling. In small animals this involves labor-intensive manual withdrawals that present several drawbacks. Time resolution is limited to 5-10 s between each sample, thereby affecting accuracy. Excessive amounts of blood are collected. Repeated exposure to radioactivity of those performing the sampling is also undesirable.

Therefore, we have evaluated real time measurement of the input function with a new system, the β -MICROPROBE™ (Biospace Lab, Paris). With one radiosensitive probe inserted in the femoral artery of a rat and a second placed at a remote site for use as a background control, we have obtained improved results while eliminating the drawbacks cited above.

Material and methods:

β MICROPROBE detection is based upon the conversion of β^+ (positrons) or β^- (electrons) particles in a scintillating optical fiber, and takes advantage of the limited range of β^- particles within biological tissues. For ^{18}F , 90% of measured counts derive from β^+ emitted in a sphere of 1 mm radius surrounding the sensitive tip. The scintillation light is guided through the fiber and then counted with a photomultiplier. The front-end electronics provide real-time display of the number of particles detected by each probe during the sampling time. In a typical blood measurement on a rat (see below), with a 250 μm diameter, 4 cm long probe, the signal was found to be 66 cps/mCi/ml while the background probe gave 55 cps/mCi/ml. Detector response is linear over a broad count rate range.

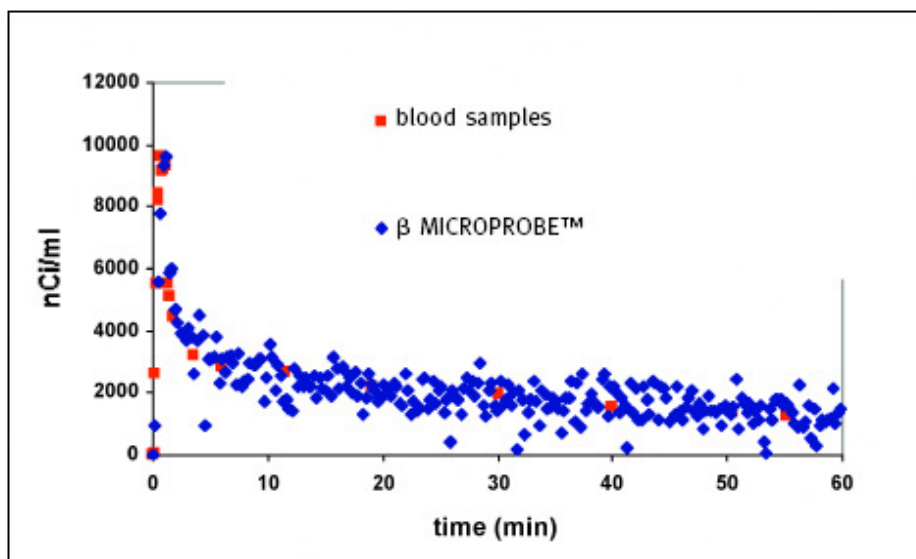


An experiment with the β MICROPROBE most often involves two probes per animal, a specific and a non-specific one, the latter used as a reference. Optionally the β MICROPROBE can be supplied with up to four probes and it is possible to monitor up to three sites simultaneously.

In the present experiment, a Sprague-Dawley rat was anesthetized by continuous I.V. administration of α -chloralose. Catheters were placed in femoral veins and arteries on the animal's left side for tracer injection and manual blood sampling. On the right side, two 250 μm dia. probes were inserted respectively in the femoral artery (signal probe) and in the tissues just above the artery (non-specific probe). The latter is used to measure the background signal for suppression. 0.3 to 1mCi ^{18}F FDG (1mL over 60s) were intravenously administered to the animal and blood activity was monitored via the β MICROPROBE and by blood sampling.

Results:

In the following figure, the signal from the β MICROPROBE, after background suppression and decay correction, is displayed together with the results from discrete blood sample measurements. The β MICROPROBE data are normalized on a late blood sample to convert the measured counts per second into nCi/ml. Results are in good agreement with the input function simultaneously derived from manual blood sampling. The 1 second time resolution ensures that the peak is not missed as sometimes observed with sampling. Since the plasma to blood radioactivity ratio vs. time is very similar from one animal to another, it is possible to obtain the plasma input function from the β MICROPROBE measurements.



Conclusion:

The sensitivity of the technique allows to monitor the input function even late into an experiment when the radioactivity level in the blood has considerably decreased. As the technique eliminates blood collection, it facilitates quantitative modeling for radio-tracer studies in small animals. The 4-probe capability makes it possible to parallel studies of on-line blood input function with determination of intake kinetics of an organ, e.g. the brain, in the same experiment. The β MICROPROBE opens the way to simply perform quantitative molecular kinetics without the requirement for PET instrumentation.

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