PET IN DRUG DEVELOPMENT

Adriaan A. Lammertsma

Department of Nuclear Medicine & PET Research, VU University Medical Center, Amsterdam, Netherlands

ABSTRACT

Positron emission tomography (PET) is a tomographic imaging technique that allows for accurate non-invasive in vivo measurements of regional tissue function in man. It is the most selective and sensitive imaging modality able to measure molecular pathways and interactions in vivo at a picomolar level.

PET is an important tool in drug development and can be used in different ways. Firstly, it is possible to label the drug itself with a positron emitter. This enables direct measurements of tissue drug concentrations, allowing for an assessment whether these concentrations are high enough for therapeutic purposes. An example is the uptake of labelled anti-cancer drugs in tumours, which can be compared with uptake in normal tissue (toxicity).

Secondly, it is possible to measure perfusion or metabolism following or during treatment. Examples are measurements of tumour perfusion following anti-angiogenesis treatment and tumour glucose metabolism as a marker of response to chemotherapy. The latter is now accepted as a surrogate endpoint in trials with new anti-cancer drugs.

Finally, receptor occupancy and enzyme inhibition can be measured using established radioligands for the molecular targets under investigation. The advantage of this approach is that it does not require novel radiochemistry or kinetic models. Receptor occupancy or enzyme activity can be measured as function of administered drug dose and biological clearance of the drug can be measured by performing scans at various times after drug administration. Both optimal dose and dosing regimen can be determined from studies with less than ten subjects.

PET studies can be performed not only in patients, but also in animal models of disease. Since PET is non-invasive, it is possible to perform repeat measurements in the same animal. This is a major advantage as an experimental animal can be used as its own control.

Index Terms— Positron Emission Tomography (PET), radiolabelling, receptor occupancy, clinical trials, drug development