Chapter 45
Pharmacokinetic Challenges against Brain Diseases with PET

Hiroshi Watabe
Graduate School of Medicine, Osaka University, Japan

Keisuke Matsubara
Akita Research Institute of Brain and Blood Vessels, Japan

Yoko Ikoma
Karolinska Institute, Sweden

ABSTRACT

Positron emission tomography (PET) is an imaging technology used to visualize distribution of particular ligands inside living organisms. The ligand is labeled by a positron-emitting isotope, such as ^{11}C, ^{15}O, ^{13}N and ^{18}F, and injected into subjects. By detecting γ-rays emitted from the ligand, in vivo biodistribution and kinetics of the ligand can be depicted with high sensitivity. By altering the target ligand for PET, one can see different distributions and time courses of the target. PET provides several biological and functional images inside the body, rather than simply an anatomical image. Therefore, PET can potentially detect biological changes that occur long before anatomical changes begin. PET has been widely used for neuroreceptor and neurotransmitter studies by tracing radioligands, which have selective affinity for a particular site. For example, the dopamine and serotonin receptors are highly related to brain disorders. By analyzing the pharmacokinetics of these ligands using PET, it is possible to noninvasively detect abnormalities in the brain. However, signals from PET contain many different types of information, and it is important to interpret the signals appropriately and choose the proper technique to analyze PET data. This chapter discusses several analytical methods for PET data.

INTRODUCTION

Positron emission tomography (PET) is an advanced imaging techniques used to visualize the interior of living bodies. PET scanning is initiated by the injection of a specific ligand labeled by a radioisotope, such as ^{11}C, ^{13}N, ^{15}O and ^{18}F, that emits positrons (we call this ligand a 'radioligand'). Each positron annihilates an electron, and two γ rays of 511 keV energy are simultaneously emitted in opposite directions. The two emitted photons are detected by γ-ray detectors in coincidence. The line connecting the two detectors is called the line-of-response (LOR), which encompasses the source of

DOI: 10.4018/978-1-4666-5125-8.ch045

the photons. By combining multiple LORs with a mathematical image reconstruction algorithm, a tomographic image of the three-dimensional distribution of the radioligand can be generated. A contemporary PET system uses a scintillation crystal, such as bismuth germinate (BGO), lutetium oxyorthosilicate (LSO), or gadolinium orthosilicate (GSO), as the γ-ray detector, and the scanner is ring shaped with more than 10,000 small pieces of scintillation crystals cylindrically aligned (see Figure 1). The half life (time for the specific activity of the radioisotope to decrease by half) of the positron-emitted radioisotope used in PET is usually short (2 min for ^{15}O, 10 min for ^{13}N, 20 min for ^{11}C, and 110 min for ^{18}F). Thus, it is necessary for each site to have a cyclotron (Figure 2) to generate the radioligand. One advantage of PET is the ability to employ radioligands that are molecular analogs of ligands naturally present inside the human body.

By visualizing the three dimensional distribution and time course of the radioligand by PET, we can noninvasively obtain information of the injected radioligand. Note that depending on the radioligand, PET scanning can sometimes last for a few hours, and a patient must lie in a fixed position during the scan. It is difficult to ask children and patients with dementia not to move during the scan, and motion correction techniques must be considered when using PET (Woo et al., 2004). The image obtained by PET represents certain functions related to the injected radioligand. For instance, images of ^{15}O -water are related to blood flow, and images of ^{11}C–raclopride, which is an antagonist for the D2 dopamine neuroreceptor, represent the map of the D2 dopamine neuroreceptor inside the body. Therefore, by altering the radioligand, we are able to measure different functions related to the ligand (Table 1). Although the spatial resolution of the PET scan-

Figure 1. Photograph of the inside of a PET scanner. It consists of a ring-shaped gantry with many scintillation crystals.

Figure 2. Photograph of the inside of a cyclotron. The cyclotron generates a proton or deuteron beam, which collides with the appropriate target (for example, water with enriched ^{18}O to generate ^{18}F).