Chapter 29

Quantitative Analysis of Amyloid β Deposition in Patients with Alzheimer’s Disease Using Positron Emission Tomography

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DOI: 10.4018/978-1-60960-559-9.ch029
ABSTRACT

Positron emission tomography (PET) is a sensitive technique for functional and molecular imaging. In Japan, the incidence of cognitive disorders is increasing at an accelerated pace, partly due to the increasing size of the elderly population. Basic and clinical studies on dementia have become very important. In vivo detection of amyloid beta (Aβ) deposits could be useful for early diagnosis of Alzheimer’s disease (AD). “Aβ imaging” by PET has been recognized as one of the most important methods for the early diagnosis of AD. Clinical PET studies have been conducted using several probes, such as [18F]FDDNP, [11C]SB-13 and [11C]Pittsburgh compound-B ([11C]PIB). [11C]PIB is the most commonly used probe.

In this chapter, a novel imaging probe, 2-[2-(2-dimethylaminothiazol-5-yl)-ethenyl]-6-[2-(fluoro)ethoxy]benzoxazole ([11C]BF-227), is reported. To the authors’ knowledge, [11C]BF-227 is the first Aβ imaging probe to be used in Japan. The purpose of this chapter is to examine methods for quantitative analysis of Aβ deposition in the human brain using PET and [11C]BF-227. Six AD patients and six healthy control subjects were used in the present study. Dynamic PET images were obtained over 60 min. Blood samples were obtained from the radial arteries.

The results were analyzed using Logan graphical analysis and full kinetic analysis. A significantly higher distribution volume ratio (DVR) value was observed in AD patients in cortical regions, e.g., the cingulate, frontal, temporal, parietal and occipital regions, than in control subjects. Satisfactory correlation of these values to the semiquantitative standardized uptake values (SUV) was obtained.

These findings suggest that [11C]BF-227 is a promising PET probe for clinical evaluation of early Aβ deposition in AD patients.

INTRODUCTION

Positron Emission Tomography

Positron emission tomography (PET) is a technique used for functional and molecular imaging based on nuclear medicine technology. Nuclear medicine techniques date back to the early 20th century. Nuclear medicine was originally developed as a “tracer technique” by the Nobel laureate, Dr. George de Hevesy. In our study, the term “tracer” means an extremely small amount of radioisotope that is administered to the subject to permit imaging certain biological phenomena in the living body. A tracer is sometimes also called a “probe”. Probes detect the presence of a certain biological substances in small amounts (often at the “nano-” to “pico-” molar scale) (Tashiro, 2010). The tracer technique was later established as a nuclear medicine technique in the late 20th century, mainly due to advancements in radiolabeling techniques and signal detection devices such as PET.

Using PET, a wide range of biological information can be obtained from the living human brain, such as the cerebral metabolic rate of glucose (CMRglc), regional cerebral blood flow (rCBF) and pharmacokinetic information regarding receptor-transmitter interactions such as those in the dopaminergic and histaminergic neuronal systems (Yanai & Tashiro, 2007; Tashiro, 2010). CMRglc is often measured using a radioactive analogue of glucose, [18F]fluorodeoxyglucose ([18F]FDG). In brain regions that have increased glucose consumption, an increased demand for glucose and oxygen causes dilation of cerebral capillaries, which can be measured as an increase in the regional cerebral blood flow (rCBF) (Tashiro, 2008). The rCBF is measured using radiolabeled water ([15O]H2O), though other radiation-free
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