S29-3 PET Probe Development for Visualization of Neuropathological features

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Due to the fact that the number of patients with dementia is growing rapidly as the World's population ages, there is an urgent need to establish a reliable method for early diagnosis of Alzheimer's disease (AD), which is a main cause of dementia in the elderly. To diagnose disease with high accuracy (sensitivity and specificity), it is necessary to detect the specific pathological features sensitively. As for AD, senile plaques and neurofibrillary tangles are formed in the brain as the hallmarks of AD pathology even in the presymtomatic phase of the disease. These hallmarks are composed of insoluble aggregates of amyloid-β (Aβ) and phosphorylated tau, respectively. Thus, they are highly expected to be reliable biomarkers for an early diagnosis of AD, if they can be measured non-invasively by imaging. Aiming at accurate and early diagnosis of AD using positron emission tomography (PET), we have been working on the development of PET probes that bind to those pathological aggregates. Especially, we succeeded to develop amyloid imaging probes, [^{11}C]BF-227 and [^{18}F]FACT, available for clinical PET through optimization of 2-arylethenyl benzoxazole derivatives. Both probes shows not only excellent binding affinity and selectivity for Aβ aggregates and senile plaques, but also good brain pharmacokinetic properties required for brain PET imaging, such as high brain uptake, smooth washout from brain, and low non-specific binding. In this lecture, I will take those amyloid imaging probes as examples how to develop PET probes from chemistry to clinical applications and mention the importance and future prospects of such research.