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Improvement of synthesizing material and method for an in-house production of [18F]-florbetapir PET tracer for imaging beta amyloid deposition in the brain

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• Background/Goal/Objective of the study;
Recently, the (E)-2-(2-(2-(2- [18F]-fluoroethoxy)ethoxy)ethoxy)-5-(4-methylaminostyryl) pyridine) (a.k.a. [18F]-florbetapir) was developed in our laboratory as a radiotracer to detect β amyloid deposition in the brain using PET scan assisting for diagnosis of Alzheimer's disease. In this research, we aimed to compare the production yield of [18F]-florbetapir obtained from the newly adapted synthesizing materials with optimized method and that of the original method.
• Methodology;
[18F]-florbetapir was produced at Siriraj Cyclotron Centre using HM-20S cyclotron with CFN-MPS200 module (Sumitomo, Tokyo, Japan). The activated fluoride (18F) was combined to AV-105 precursor by substituting the tosylate leaving group in a fluorination step. Then, 1N hydrochloric acid was added and pH-adjusted with 1N sodium hydroxide to remove the boxylic protecting group with de-protection process or hydrolysis. During synthesizing steps, in the original method (Method A) we used FLT cassette (Sumitomo, Tokyo, Japan) with installed silicone tubes. In the new method (Method B), we replaced all original tubes in FLT cassette with PharMed® BPT tube (Saint-Gobain, Akron Ohio, United States), which was further sent for sterilization at local central sterile supply department (CSSD) before use. Following purification via HPLC semi-preparative, the products from both methods were neutralized with 0.5% sodium ascorbate/water (non-diluted in method A and diluted 1:8 in method B), purified with Sep-Pak tC18 reverse phase column, eluted into the vial containing normal saline and filtrated with 0.22 μm Millex GV filter.
The quality control of [18F]-florbetapir was done by standard methods for the determination of basic characteristics of radiopharmaceuticals including appearance, acid-base range, radio chemical purity, residual solvent, pyrogenicity, half-life, chemical impurities, sterility, nuclidic purity and assay of ascorbic acid. The remaining radioactivity inside the tubes, overall yield, specific activity, radiochemical purity and other physical properties from both methods were compared.
• Results and Discussion;
The remaining radioactivity inside the tubes of method B was 3.23±1.4 (n =4), which was 32.57% decreased from 9.93±1.52% remaining radioactivity in the tubes of method A (n = 3). The recovery rate from tC18 after neutralization with 0.5% sodium ascorbate/water (Method B) was 94.72±6.00%, which was higher than 76.71±4.58% from method A.
The overall yield, specific activity and radiochemical purity of [18F]-florbetapir produced by method B were 21.4±0.2% (not decay corrected), 5.24±2.25 TBq/mmol and 96.1±3.2%, respectively, which were higher than 5.7±1.50%, 1.26±0.28 TBq/mmol and 95.84±0.80% obtained from method A. Other physical properties including appearance, acid-base range, half-life, residual solvents (acetonitrile and DMSO), total chemical impurities, assays of ethanol and assays of sodium ascorbate, and bacterial endotoxins of [18F]florbetapir produced by both methods were within standard criteria.
• Conclusion;
We successfully improved [18F]florbetapir production by optimizing new type of tubing cassette material to use with the automated synthesizer and minor adjustment of neutralization method. This new method provides higher production yield and higher radiochemical purity as compared to our previous method. In addition, this applied cassette is able to reduce production cost, easy to operate and suitable for Siriraj Cyclotron facility.

Primary author: SIRIPRAPA, TOSSAPORN (Faculty of Medicine Siriraj Hospital)

Co-authors: Dr NAKA, Sadashiro (Osaka University Hospital); THIENTUNYAKIT, Tanyaluck (Siriraj Hospital)

Presenter: SIRIPRAPA, TOSSAPORN (Faculty of Medicine Siriraj Hospital)