Accepted presentation (#1476) in the SNM 59th Annual Meeting 2012 Miami, Florida/US

Fully automated synthesis of ^{18}F-FET using the Synthera® Platform

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Objectives

The most widely used radiopharmaceutical in oncology, ^{18}F-FDG, is relatively suboptimal for detecting tumors in the brain due to the glycolytic metabolism in the normal cortex, which causes low target-background ratios. Amino acid transport utilizing radiolabeled amino acids has shown higher sensitivity in the evaluation of brain tumors, the most widely used being *O*-(2-[^{18}F]fluoroethyl)-L-tyrosine (^{18}F-FET). The automated synthesis of ^{18}F-FET was here optimized on the Synthera® Platform comprising a synthesis module coupled to an HPLC unit (IBA Molecular, Belgium). The aim was to establish a reliable synthesis with high radiochemical yield using the FDG configuration setup (IFP™).

Methods

The TET precursor ((2S)-O-(2-tosyloxyethyl)-N-trityl-tyrosine-*tert*-butyl ester) was purchased from ABX (Germany). ^{18}F-FET was synthesized by nucleophilic substitution of tosylate by [^{18}F]fluoride and subsequent hydrolysis of the tButyl-ester protecting group ($CHCl_3$/TFA: 4/1) using a standard disposable FDG cassette (IFP Nucleophilic). Purification was done by HPLC on an Apollo 250x10 mm C18 5 µm column using H_2O:EtOH (95/5) as eluent at a flow rate of 6 ml/min. Reaction parameters such as reaction time and temperature of fluorination and deprotection were optimized in order to obtain an acceptable radiochemical yield. Quality control was done by HPLC analysis of the final product on a C18 Prevail column with H_2O:EtOH (90/10) at 1ml/min.

Results

^{18}F-FET was produced in 25-30% yield non-decay-corrected (40% decay-corrected) and with a radiochemical yield >95% after ± 66 minutes of radiosynthesis including HPLC purification and formulation.

Conclusions

A fully automated, reproducible process for ^{18}F-FET synthesis was developed using an IBA SynthERA synthesis module. This one pot two-step procedure is a convenient and reliable method to prepare ^{18}F-FET in a reproducible yield with high radiochemical purity.
This process could be applied for routine GMP PET production for clinical applications.