Fully automated production of [^{18}F]fluoroacetate on IBA Synthera platform

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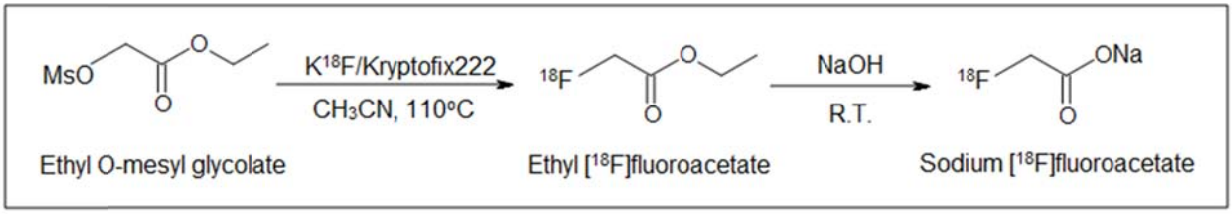
Objectives: F-18 labeled fluoroacetate ([^{18}F]FA) has been developed as a PET radiopharmaceutical of acetate metabolism imaging[1-2]. An IBA Synthera is distributed as a compact synthesizer which has disposable cassette concept including one reaction pot and four reagent vials. In the ISRS2011 (Amsterdam) meeting, we reported the automated synthesis of [^{18}F]FA using the Synthera, however, it included a troublesome HPLC purification process for routine production[3]. In this study, we developed and optimized fully automated synthesis without the HPLC process.

Methods: The synthesis of [^{18}F]FA was modified from the method of Sun et al.[4] (Scheme 1). Limited four reagents were selected as follows: (**a**) kryptofix2.2.2./K_2CO_3 mixture, (**b**) ethyl *o*-mesyl-glycolate as a precursor, (**c**) 1M NaOH, (**d**) sterile water. In addition, we employed 3 pieces of Waters Oasis HLB cartridges to purify an intermediate, ethyl [^{18}F]FA and perform following hydrolysis. No-carrier-added [^{18}F]fluoride in irradiated ^{18}O water was trapped on a Waters Sep-Pak QMA light cartridge, and the [^{18}F]fluoride was eluted with different amounts of **a** in 0.6 ml of 95% acetonitorile/water. The eluate in a reactor was azeotropically evaporated at 110°C for 5 min under nitrogen gas flow. Then, 15 or 5 mg of **b** in 1 ml of anhydrous acetonitrile was added to the reactor and the labeling was conducted at 110°C for 5 min in sealed condition. After cooling for 3 min, the hydrolysis was performed on 3 pieces of HLB with 1 ml of **c** at room temperature for 10 min. Finally, the solution was transferred to a sterile vial including citrate buffer via an HLB, an almina cartridge and 0.22μm filter.



Scheme 1. Synthesis of [^{18}F]fluoroacetate

Results: As a result of decreasing the amount of a precursor from 15 mg to 5 mg in labeling process, it did not have significant difference on the yield of fluorination. We also confirmed that the amount of K_2CO_3 was remarkably influenced of the yield of ethyl [^{18}F]FA and smaller amount of that was suitable for the purification step. The optimized procedure was achieved with a high and reproducible radiochemical yield exceeding >50% (decay corrected) within less than 40 min. The radiochemical purity of the final product was greater than 95%.

Conclusions: The automated synthesis of [^{18}F]FA without HPLC process using Synthera has been accomplished. This work helps easy access to [^{18}F]FA production for PET imaging.

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