Fully automated and GMP-compliant synthesis of [^{18}F]JK-PSMA-7 on a Trasis AllinOne module

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Objectives:

Positron emission tomography (PET) imaging with probes targeting prostate-specific membrane antigen (PSMA) is widely used for the clinical diagnosis and staging of prostate cancer in men [1, 2]. Recently disclosed [^{18}F]JK-PSMA-7 ([^{18}F]**3**) has shown favorable properties for tumor detection after biochemical recurrence [3, 4]. In the present work, we established a robust and fully GMP-compliant process for the automated radiosynthesis of [^{18}F]**3** on a Trasis AllinOne (AIO) synthesizer.

Methods:

To simplify implementation on an automated synthesis module, the radiosynthesis of [^{18}F]JK-PSMA-7 was devised as a one-pot, two-step reaction that comprises i) an ^{18}F-for-N^{+}(CH$_3$)$_3$ exchange reaction using the highly-activated 6-methoxy-*N,N,N*-trimethyl-5-(2,3,5,6-tetrafluorophenoxycarbonyl)pyridine-2-aminium triflate **1** as radiolabeling precursor, and ii) a de-protection step using non-toxic ortho-phosphoric acid to hydrolyze the *t*Bu-protecting groups of the radiolabeled intermediate [^{18}F]**2** (**Figure 1**).

The automated process started with elution of [^{18}F]fluoride from a QMA cartridge with a solution of tetrabutylammonium hydroxide in MeCN/H$_2$O, followed by three azeotropic drying steps at different temperatures. Precursor **1** (10 mg) was automatically dissolved in 1 mL MeCN and added to the dried [^{18}F]fluoride, after which the ^{18}F-for-N^{+}(CH$_3$)$_3$ exchange reaction proceeded for 5 min at 70 °C. 1 mL of ortho-phosphoric acid was then directly added into the reactor and the reaction mixture was heated for 5 min at 70 °C to convert [^{18}F]**2** into [^{18}F]**3**. After cooling and dilution with saline, the raw solution was directly transferred to an HPLC system for purification of [^{18}F]**3**.

Results:

The average non-decay corrected yield of [^{18}F]JK-PSMA-7 ([^{18}F]**3**) produced using the AIO system was 38.9 ± 4 % (n = 260; radiochemical yield of 58 %), with an overall synthesis time of about 1 h. In a single production batch starting from 36-43 GBq, between 13-19 GBq of [^{18}F]**3** with a radiochemical purity of > 99 % could be produced. Quality control test were fully compliant with the acceptance criteria defined by the European Pharmacopoeia specifications for the synthesis of ^{18}F-labeled radiotracers.

Conclusions:

The use of a cassette system simplifies the GMP-compliant preparation of [^{18}F]JK-PSMA-7, eliminates the risk of cross-contamination, greatly minimizes the risk of operating errors and increases the reliability of the syntheses.

References:

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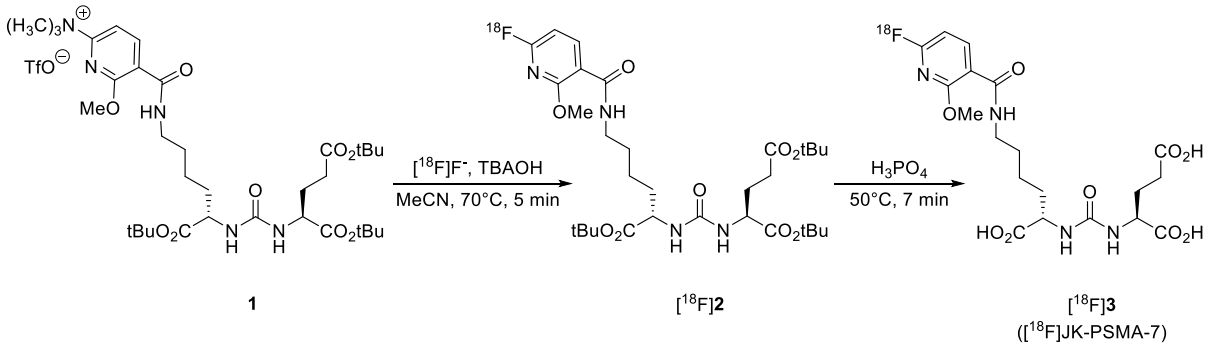

1 [^{18}F]**2** [^{18}F]**3** ([^{18}F]JK-PSMA-7)

Figure1: Synthesis of [^{18}F]JK-PSMA-7 ([^{18}F]**3)** by a direct one-pot two-step synthesis.