Optimisation of the automated synthesis of ^{18}F-FMISO using the Synthera® Platform

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Objectives

Demonstrating tumor hypoxia *in vivo* in a non-invasive manner by 18F-FMISO-PET can be used to predict resistance to radiotherapy [1]. The automated synthesis of ^{18}F-FMISO (^{18}F-Fluoromisonidazole) was 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™) and a reduced amount of precursor (5 mg).

Methods

The NITTP precursor(1-(2'-nitro-1'-imidazolyl)-2-O-tetrahydropyranyl-3-O-toluenesulfonylpropanediol) was purchased from ABX (Germany). ^{18}F-FMISO was synthesized by nucleophilic substitution of tosylate by [^{18}F]fluoride and subsequent acidic hydrolysis of the tetrahydropyranyl-protecting group (Fig.1) using a standard disposable FDG cassette (IFP Nucleophilic) [2]. Purification was done by HPLC on a VYDAC 250x10 mm C18 10 µm column using H_2O:EtOH (92/8) as eluent at 4 ml/min. Reaction parameters such as reaction time (3-20 min) and temperature (100-145°C) of fluorination were altered in order to optimise the radiochemical yield when using only 5 mg of precursor.

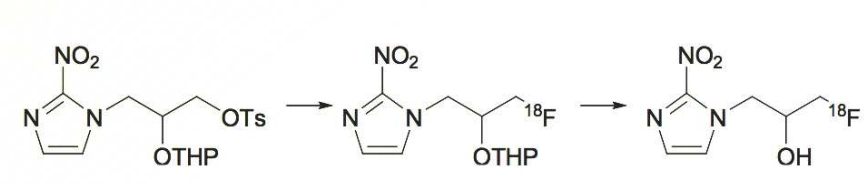

Fig.1 Synthesis route of ^{18}F-FMISO

Results

Prolonging the fluorination time did not improve labeling efficiency. In contrast, raising the reaction temperature to 120°C clearly lead to higher yields up to 50% (decay corrected) when using 5 mg of the NITTP precursor. Above 120°C, the yield did not increase further and an intermediate side product was sometimes observed. Reaction times of fluorination could be shortened to 3 minutes at 120°C so that total synthesis including HPLC purification was completed in 40 minutes. The radiochemical purity determined by HPLC was >97%.

Fig.2 Synthera HPLC printscreeen of the main page

Conclusions

We were able to synthesize and purify ^{18}F-FMISO in a reliable routine production manner on the Synthera® platform using the FDG-IFP™ configuration. Yields up to 50% were obtained with 5 mg precursor, which is acceptable although lower compared to 70-80% that can be achieved with the use of 10 mg NITTP.

Research Support

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References.

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