Improved automated synthesis of [^{18}F]FECh as a radiotracer for prostate cancer imaging

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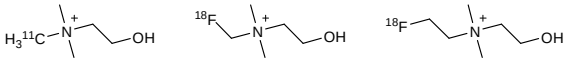
Introduction: Many tumours are characterized by an enhanced cell proliferation. This is normally associated with an elevated uptake and phosphorylation of choline to form phosphoryl choline, which is used in the synthesis of membrane phospholipids.
Therefore [^{11}C]choline was developed and has shown its potential by evaluation of brain tumours, esophageal carcinoma and prostate carcinoma.[1-3] Because of the short half-life of ^{11}C ($T_{1/2}$ = 20.3 min), resulting in a limited usefulness for clinical routine, different ^{18}F-labelled ($T_{1/2}$ = 109.7 min) analogues were synthesized to overcome this problem. Shown in figure 1 are the most prominent choline derivatives:



(1) (2) (3)

Fig. 1:
Structure of [^{11}C]choline (1) and the fluorinated analogues [^{18}F]fluorocholine (2,) and [^{18}F]fluoroethylcholine (3, FECh)

GE Medical System. Because of the different labelling techniques of ^{11}C and ^{18}F the module had to be modified. Hence the cooling, the heating and some valves and tubes had to be rearranged, resulting in the module shown in figure 2.
[^{18}F]FECh was prepared in a two step synthesis, via a ^{18}F-fluoroethylation using [^{18}F]FETos. In the first step [^{18}F]fluoride was dried and reacted with ethylenglycol-1,2-ditosylate to yield [^{18}F]FETos. The crude product then was diluted with water, loaded on a Lichrolut EN column and eluted using DMSO. Afterwards this solution was reacted with N,N-dimethylaminoethanol for 20 minutes using alkali iodide catalysis, then diluted with water and purified with a LiChrolut SCX column and HPLC to yield the [^{18}F]FECh.
This synthesis results in a total radiochemical yield of 20-25 % within 50 min. The identity of [^{18}F]FECh was confirmed by gradient HPLC, by comparing the radiochromatograms with chromatograms of the unlabelled FECh, showing a radiochemical purity of over 95%.

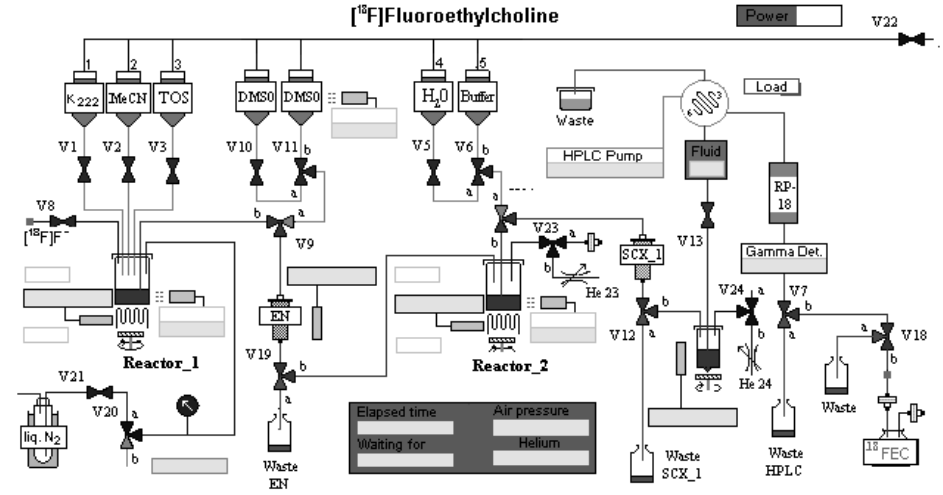


Fig. 2: Diagram of the automated synthesis module for the production of [^{18}F]FECh

Considering the isotope properties, complexity of synthesis and biochemical behaviour of the derivatives, [^{18}F]FECh seems to be the most promising candidate for clinical PET studies. Hence there is a high interest in a reliable, fully automated synthesis for the production of [^{18}F]FECh.
Recently we reported that the addition of alkali iodides to 2-[^{18}F]fluoroethyltosylate ([^{18}F]FETos) and 1-bromo-2-[^{18}F]fluoroethane led to drastically increased radiochemical yields most probably due to the *in situ* formation of 1-iodo-2-[^{18}F]fluoroethane.[4] We therefor developed a new approach for a fully automated synthesis for the production of [^{18}F]FECh, using the iodide promoted alkylation, which circumvents the problems of the one-pot strategy.

Results: The automated radiosynthesis of [^{18}F]FECh was performed by using a module for ^{11}C-methylation from

Conclusion: After optimization and automation of this iodide promoted ^{18}F-fluoroalkylation of N,N-dimethylaminoethanol, a fast and reliable high-yield synthesis of [^{18}F]fluoroethylcholine was developed, which can be accomplished by a modified commercial available module. This is especially important when large amounts of [^{18}F]fluoroethylcholine, for example in PET studies, are needed.

References:

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