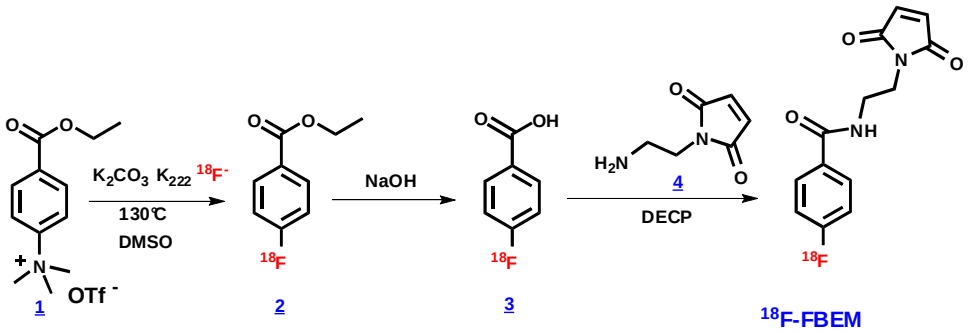
Automated synthesis of [^{18}F] FBEM for labeling of thiol containing compounds

Paris Jérôme[1], Thonon David[1], Goukens Eve[1], Kaisin Geoffroy[1], Goblet David[1], Lacroix Simon[2] and Luxen André[1]
[1] Cyclotron Research Center, Université de Liège, Belgium
[2] Erasme Hospital, PET-SCAN Unit, Bruxelles

Objectives : [^{18}F]FBEM, i.e. *N*-[2-(4-[^{18}F]fluorobenzamido)ethyl]maleimide, is a useful synthon employed for the specific radiolabeling of thiol containing compounds, including peptides and proteins [1]. The aim of the present work was to develop a fast, reproducible and fully automated synthesis of this compound in order to improve its availabilty as well as for obvious radioprotection matters.

Methods : A three-step synthetic pathway was followed (scheme 1) and implemented on a GE FastLab^{TM} system by modifying the original [^{18}F]FDG sequence and reagents cassette configuration. The process starts with the [^{18}F] F$^-$ nucleophilic substitution of the trimethylammonium ethylbenzoate compound 1 followed by NaOH hydrolysis performed in the same labeling reactor [2]. After acidification (HCl 0.25M), the resulting [^{18}F]Fluorobenzoic acid 3 was trapped and purified on a solid phase extraction cartridge before being coupled to amino-maleimide compound 4 in the next step. This was carried out using diethylcyanophosphonate [3] in acetonitrile at 70°C. Then [^{18}F]FBEM could be isolated and purified on a second SPE cartridge.



Scheme 1 : Radiosynthesis of [^{18}F]FBEM

Results : The fully automated process takes around 55 minutes and the desired product is obtained with a decay-corrected radiochemical yield of 41 % (n=11) and a radiochemical purity ≥ 90 % as determined by HPLC and TLC. Subsequent conjugation to thiol containing compounds was also carried out.

Conclusions : A completely automated radiosynthesis of [^{18}F]FBEM has been developed with good radiochemical yields and purity**.** The resulting SPE purified maleimide synthon is suitable for the labeling of various thiol containing compounds under mild conditions.

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References : [1] D.O. Kiesewetter, et al., (2008) *J. Fluorine Chem.129*, 799-806. [2] D.Thonon, et al., (2011) *Mol. Imaging Biol.*, DOI : 10.1007/s11307-011-0470-x. [3] .O. Kiesewetter, et al., (2011) *Applied Rad. Isotopes* 69, 410-414