



Automated microfluidic synthesis of N-succinimidyl 4-¹⁸F fluorobenzoate: a protein labelling agent

Tutar R.^a, Shalgunov V.^b, Elsinga P. H.^b, Sönmezoğlu K.^c

^a*Istanbul University, Engineering Faculty, Chemistry Department*

^b*University Medical Center Groningen, University of Groningen, the Netherlands*

^c*Istanbul University, Cerrahpasa Medical Faculty*

Keywords:

Microfluidic,
[¹⁸F] SFB,
protein labelling,
[¹⁸F] FB-HAS.

Corresponding author:

Rumeysa TUTAR

E-mail:

rumeysa.tutar@istanbul.edu.tr

Tel: 0 (212) 473 70 00

Fax: 0 (212) 473 21 80

Abstract: Biomolecules labeled with radioactive fluorine ¹⁸F are an invaluable tool for the molecular imaging of physiological processes with positron emission tomography (PET). N-succinimidyl 4-[¹⁸F] fluorobenzoate ([¹⁸F]SFB) is one of the most popular ¹⁸F-synthons used for the labeling of free amine groups of biomolecules². Manual synthesis of [¹⁸F] SFB is, however, laborious work and leads to excess radioactivity exposure. The use of microfluidics for automated radiosynthesis has recently gained popularity in the research community. An automated procedure of [¹⁸F]SFB synthesis has been developed starting from (4-ethoxycarbonyl)-N,N,N-trimethylbenzeneaminium triflate using a platform consisting of the microfluidic module Advion Nanotek (USA) and a conventional radiosynthetic module Nuclear Interface (Germany). To test the reactivity of the thus obtained [¹⁸F] SFB, we used it to prepare [¹⁸F] fluorobenzoylated human serum albumin ([¹⁸F] FB-HSA), a blood pool imaging agent. [¹⁸F]SFB was obtained within 90 min synthesis time (including purification) in 13±8% isolated yield and >95% radiochemical purity. Conversion of [¹⁸F] SFB into [¹⁸F] FB-HSA was 26.9 % within 30 min. Radiochemical purity of gel-filtration-purified [¹⁸F] FB-HSA was >97%. An automated synthesis procedure suitable for the preparation of [¹⁸F] SFB has been developed. This protocol can be used to label biomolecules for research purposes.

Sažetak

Biomolekule obilježene sa radioaktivnim fluorom, ¹⁸F, predstavljaju neprocjenjivo sredstvo za molekularno oslikavanje fizioloških procesa sa pozitronskom emisijom tomografijom (PET). N-sukcinimidil 4-[¹⁸F] fluorobenzoat ([¹⁸F]SFB) je jedan od najpopularnijih ¹⁸F-sintona koji se koristi za obilježavanje slobodnih amino grupa u biomolekulama². Manuelna sinteza [¹⁸F] SFB je komplikovana i praćena većem izlaganju radioaktivnom zračenju. Upotreba mikrofluida za automatiziranu radiosintezu sve više dobiva na značaju.

Automatizirana procedura za sintezu [¹⁸F]SFB je razvijena u ovom radu počevši sa (4-etoksikarbonil)-N,N,N-trimetilbenzeneaminium triflatom, koristeći platform koja se sastoji od mikrofluidnog modula Advion Nanotek (USA) i konvencionalnog radiosintetskog modula Nuclear Interface (Germany). Za testiranje reaktivnosti dobivenog [¹⁸F] SFB, pripremali smo [¹⁸F] fluorobenzoilirani ljudski serum albumin ([¹⁸F] FB-HSA), koji se koristi kao sredstvo za slikanje krvi.

[¹⁸F]SFB je dobiven unutra 90 min trajanja sinteze (uključujući prečišćavanja) sa prinosom 13±8% i >95% radiohemijskom čistoćom. Konverzija [¹⁸F] SFB u [¹⁸F] FB-HSA je iznosila 26.9 % u toku 30 min. Radiohemijska čistoća gel-filtracijom prečišćenog [¹⁸F] FB-HSA je iznosila >97%.

Automatizirana procedura za sintezu [¹⁸F] SFB je razvijena u ovom radu. Ovaj protokol se može koristiti za obilježavanje biomolekula u cilju daljnjih istraživanja.