Electronic Supplementary Material (ESI) for Lab on a Chip

Supplementary Information

Application of [^{18}F]FDG in radiolabeling reactions using microfluidic technology

Vincent R. Bouvet, Frank Wuest*

1- [^{18}F]FDG-TATE : Aminoxy-functionalized TATE and its labeling using [^{18}F]FDG.

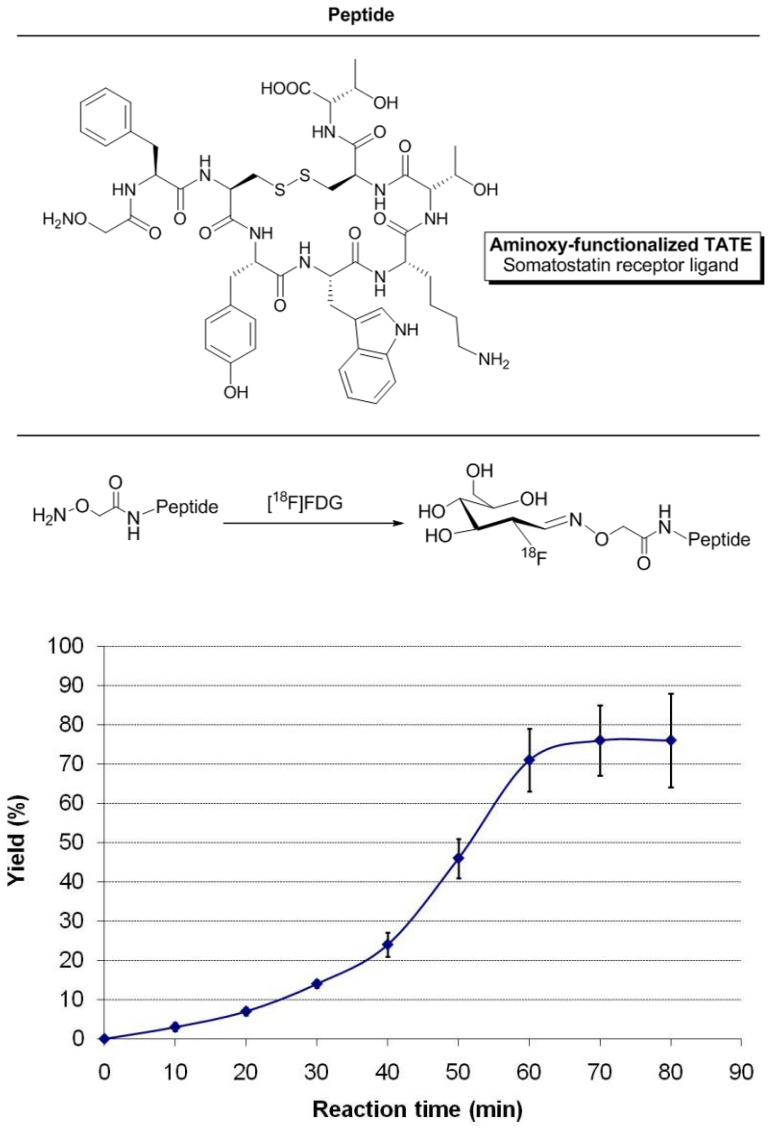


Figure S1. [^{18}F]FDG-TATE synthesis using conventional methodology. Manual labeling of aminoxy-TATE was completed in 70 min. (3.6 µmol/mL, 90 °C) 4 mg/mL in methanol.

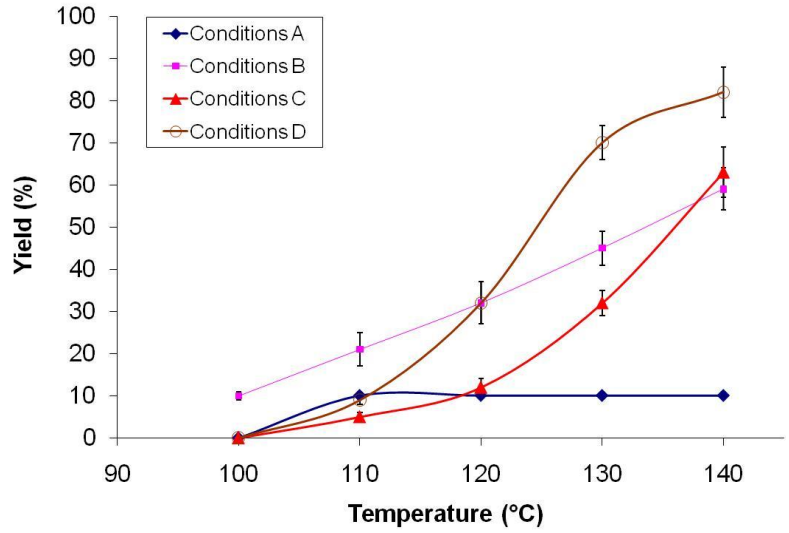


Figure S2. [^{18}F]FDG-TATE optimization using microfluidic methodology.

Condition A : 68 µg of precursor in 20 µL of MeOH, injection ratio 1, overall injection rate 10 µL.min^{-1}, reactor 4 m, residency time = 3'12".

Condition B : 68 µg of precursor in 20 µL of MeOH, injection ratio 2, overall injection rate 12 µL.min^{-1}, reactor 4 m, residency time = 2'40".

Condition C : 58 µg of precursor in 20 µL of MeOH, injection ratio 3, overall injection rate 16 µL.min^{-1}, reactor 4 m, residency time = 2 min.

Condition D : 124 µg of precursor in 20 µL of MeOH, injection ratio 2, overall injection rate 12 µL.min^{-1}, reactor 4 m, residency time = 2'40".

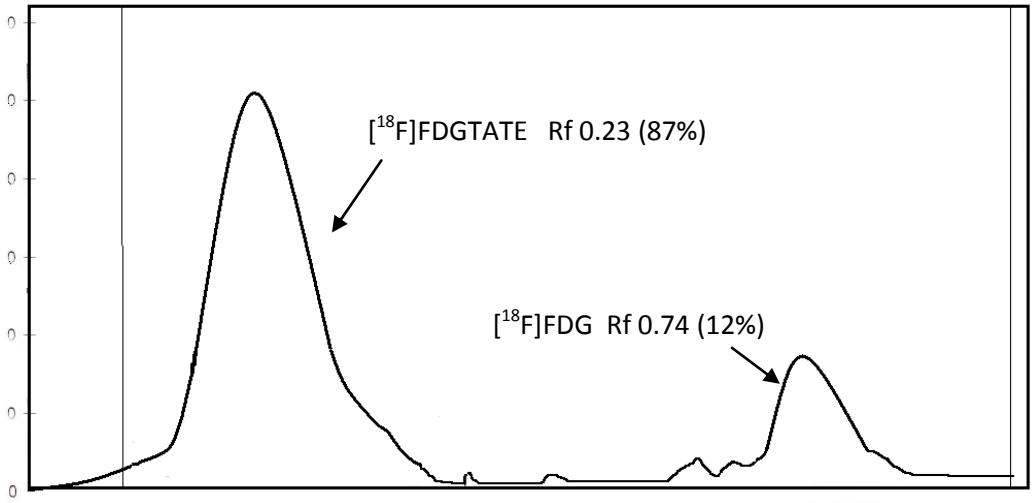


Figure S3. [^{18}F]FDG-TATE Radio-TLC. H_2O/TFA/CH_3CN (80/0.1/20)

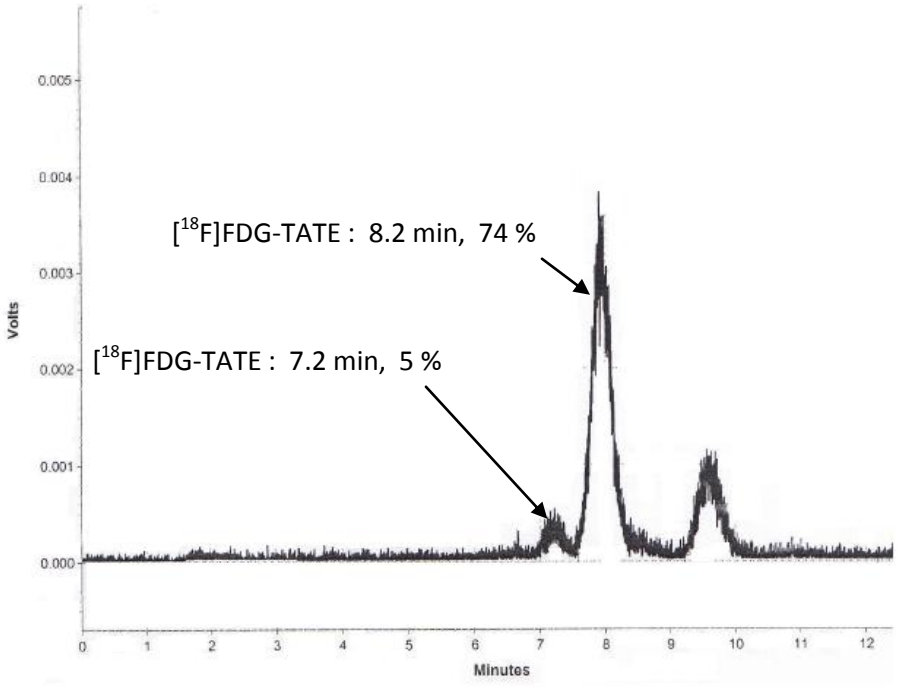
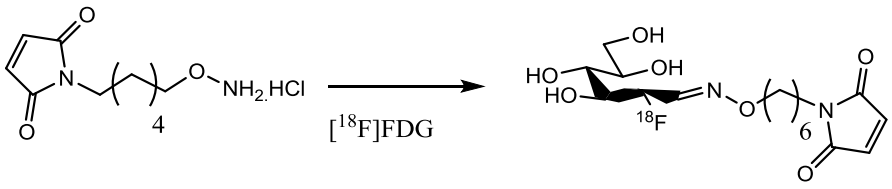


Figure S4. [^{18}F]FDG-TATE Radio-HPLC. [^{18}F]FDG-TATE was performed on a semi-preparative Luna C18 column (100 Å, 10 µm, 250 x 10 mm). The desired compound was eluted using CH_3CN/ H_2O (25/75, v/v) for 20 min at a flow rate of 4 mL.min^{-1}.

2- [^{18}F]FDG-MHO.



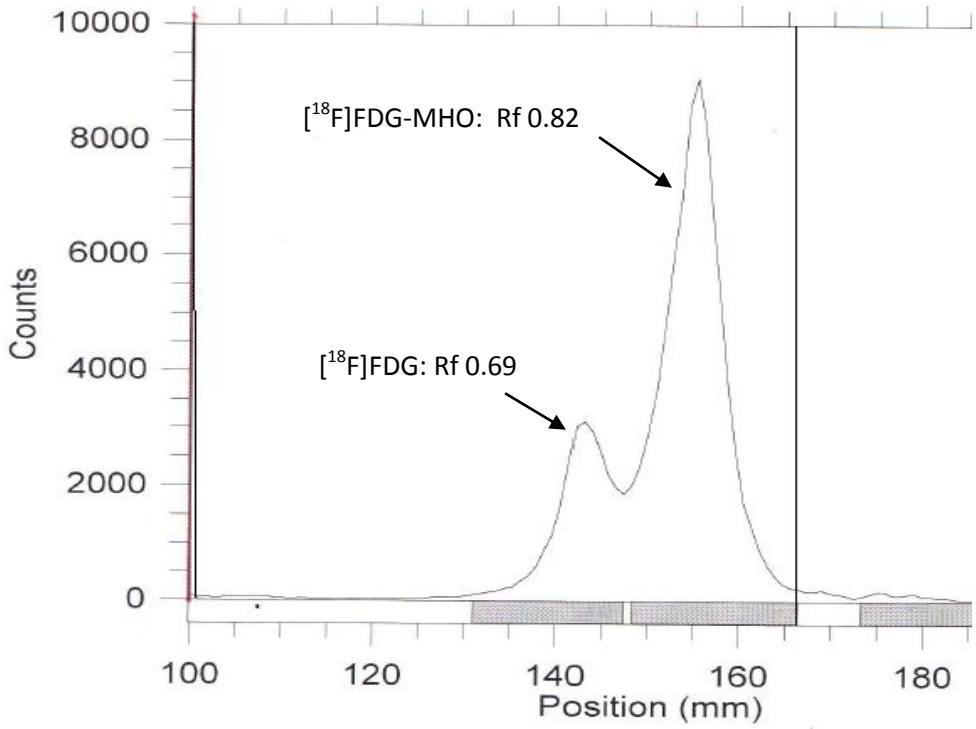


Figure S5. [^{18}F]FDG-MHO Radio-TLC. CH_3CN/H_2O (95/5)

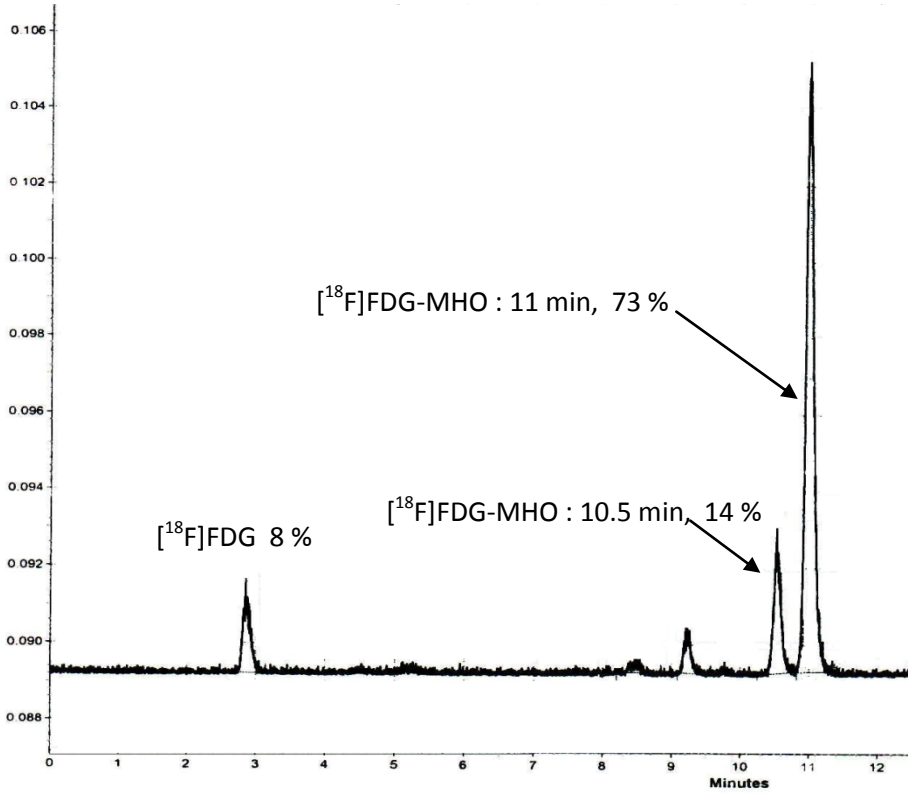


Figure S6. [^{18}F]FDG-MHO Radio-HPLC. Luna C18 column (100 Å, 10 µm, 250 x 10 mm). The eluting solvent started with a CH_3CN/H_2O gradient from (15/85 to 48/52, v/v) for 12 min at a flow rate of 4 mL.min^{-1}.

[^{18}F]FDG-MHO Optimization Tables

Table S1: Influence of the reaction temperature on the [^{18}F]FDG incorporation[a]

Entry	Temperature (°C)	Injection ratio[b]	Residency time (min)	Radiochemical yield (%)[c]
1	90	1	3'55"	16±3
2	100	1	3'55"	33±5
3	120	1	3'55"	37±2
4	130	1	3'55"	43±2 + degradations

[a] All reactions were carried out using a flow rate of 8 µL.min^{-1}, a reactor size of 4 m, and a labeling precursor concentration of 10.5 mg.mL^{-1}.
[b] Injection ratio = $V_{[precursor]}/V_{[^{18}F]}$
[c] The radiochemical yields were determined by radio-TLC

Table S2 : Influence of the flow rate on the [^{18}F]FDG incorporation[a]

Entry	Injection ratio[b]	Flow rate (µL.min^{-1})	Reactor size (m)	Residency time (min)	Radiochemical yield (%)[c]
1	2	12	4	2'40"	32±4
2	2	24	8	2'40"	64±7

[a] All reactions were carried out using a reaction temperature of 120 °C and a labeling precursor concentration of 13.75 mg.mL^{-1}
[b] Injection ratio = $V_{[precursor]}/V_{[^{18}F]}$
[c] The radiochemical yields were determined by radio-TLC

Table S3 : Influence of the injected volume ratio ($V_{precursor}/V_{[18F]}$) between the labeling precursor and [^{18}F]FDG on the radiochemical yield[a]

Entry	Injection ratio[b]	Flow rate (µL.min^{-1})	Residency time (min)	Radiochemical yield (%)[c]
1	1	16	3'55"	52±8
2	2	15	4'11"	80±5
3	3	16	3'55"	83±1

[a] All reactions were carried out using a reaction temperature of 120 °C, a labeling precursor **1** concentration of 13.75 mg.mL^{-1}, and a reactor size of 8 m.
[b] Injection ratio = $V_{[precursor]}/V_{[^{18}F]}$
[c] The radiochemical yields were determined by radio-TLC

Table S4 : Influence of the residency time on the [^{18}F]FDG incorporation[a]

Entry	Reactor size (m)	Residency time (min)	Radiochemical yield (%)[b]
1	4	2'40"	32±4
2	8	5'20"	86±2

[a] All reactions were carried out using a reaction temperature of 120 °C, a labeling precursor concentration of 13.75 mg.mL^{-1}, an injection ratio of 2, and a flow rate of 12 µL.min^{-1}.
[b] The radiochemical yields were determined by radio-TLC

Table S5 : Influence of the precursor concentration on the [^{18}F]FDG incorporation[a]

Entry	Labeling precursor concentration (mg.mL^{-1})	Radiochemical yield (%)[b]
1	1.25	0
2	5	5±3
3	10.5	35±3
4	13.75	56±6

[a] All reactions were carried out using a reaction temperature of 120 °C, an injection ratio of 2, a flow rate of 12 µL.min^{-1}, and a reactor size of 4 m (reaction time of 2'40 sec).
[b] The radiochemical yields were determined by radio-TLC.

[^{18}F]FDG-MHO Reactivity Table

Table S6 : evaluation of the microfluidic [^{18}F]FDG-MHO by coupling with GSH using a conventional manual set-up.

[^{18}F]FDG-MHO	GSH concentration						
	10 mg.ml^{-1}	1 mg.mL^{-1}	100 µg.mL^{-1}	10 µg.mL^{-1}	1 µg.mL^{-1}	100 ng.mL^{-1}	10 ng.mL^{-1}
Ref. 14 HPLC pure[a]	>95%	>95%	>95%	>95%	>95%	**92**	47
Crude[b]	**28**	11	0	0	0	0	0
HPLC pure[c]	100	100	**92**	41	8	0	0
Purified [^{18}F]FDG+HPLC[d]	100	100	100	92	75	10	0

[a] [^{18}F]FDG-MHO HPLC purified, Data extracted from Ref 14. ([^{18}F]FDG glucose amount reported (50 µg.mL^{-1}))
[b] [^{18}F]FDG-MHO isolated directly out of the microfluidic system. ([^{18}F]FDG glucose amount (~ 500 µg.mL^{-1}))
[c] [^{18}F]FDG-MHO HPLC purified after synthesis using microfluidic methodology. ([^{18}F]FDG-MHO and glucose-MHO were not separable in our conditions)
[d] [^{18}F]FDG is pre-purified using HPLC, prior to the synthesis using microfluidic methodology. ([^{18}F]FDG and glucose were not fully separable in our conditions). Then [^{18}F]FDG-MHO is HPLC purified after synthesis using microfluidic methodology.

3- [^{18}F]FDG-MHO-GSH

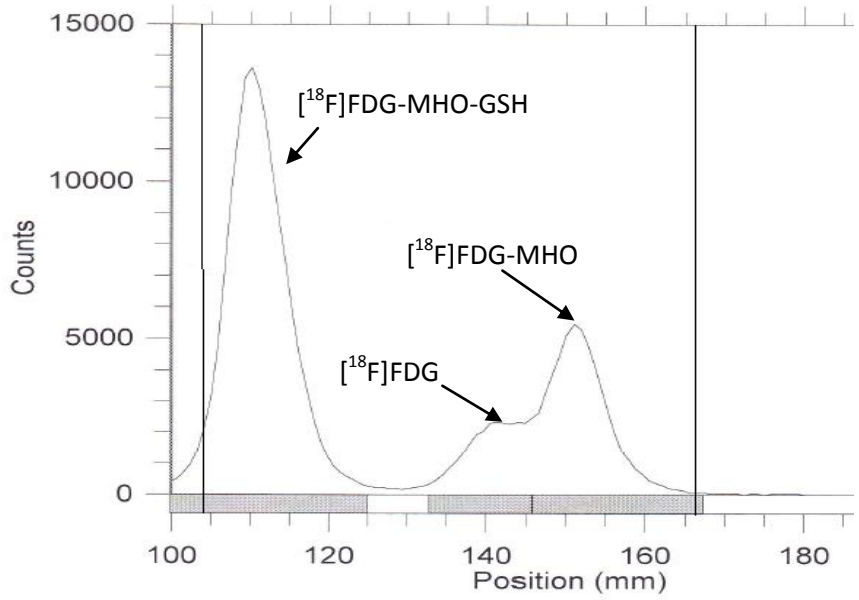


Figure S7. [^{18}F]FDG-MHO-GSH Radio-TLC. CH_3CN/H_2O (95/5)

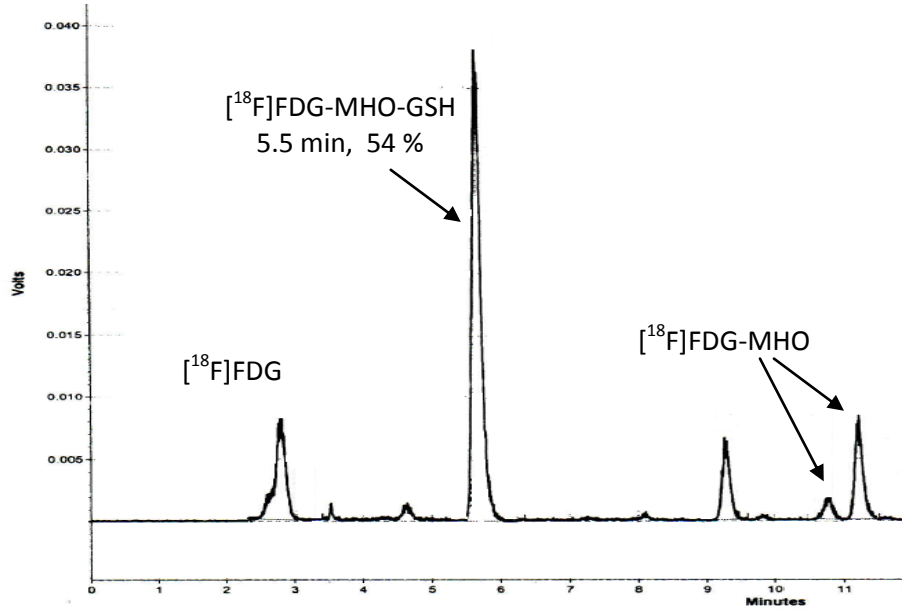


Figure S8. [^{18}F]FDG-MHO Radio-HPLC. Luna C18 column (100 Å, 10 µm, 250 x 10 mm). The eluting solvent started with a CH_3CN/H_2O gradient from (15/85 to 48/52, v/v) for 12 min at a flow rate of 4 mL.min^{-1}.