Simplified Automation of the GMP production of ^{68}Ga-labelled peptides

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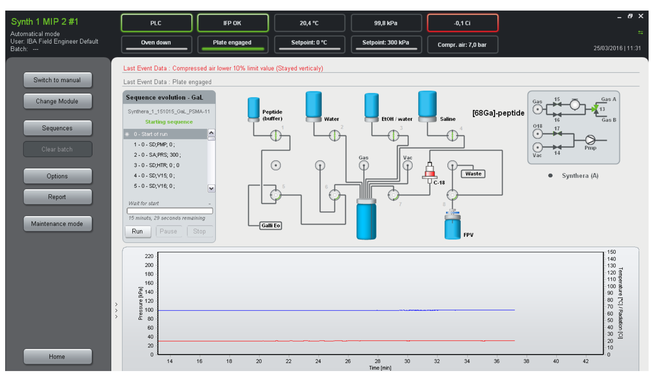
Introduction

Optimized automated process for the GMP production of ^{68}Ga-DOTA-NOC and ^{68}Ga-PSMA-11 using a cassette-based synthesizer (Synthera®, IBA, Louvain-la-Neuve, Belgium) in combination with a recently commercialized ^{68}Ge/^{68}Ga generator (Galli Eo™, IRE-Elit, Fleurus, Belgium) have been developed in this work.

Materials & Methods

Set-up in a standard hot cell: Synthera® synthesizer combined with IRE* Galli Eo™ *^{68}Ge/^{68}Ga generator



Schematic diagram depicting the automated synthesis of ^{68}Ga-labelled peptides

^{68}Ge/^{68}GaGenerator elution

-1,1 ml – 0.1 M HCl

-No pre-purification required

- Eluate sent directly to the IBA Synthera® reaction vessel

DOTA-NOC labelling

- 50 µg peptide
- acetate buffer: 1 mL 250 mM (pH 5)
- heated at 120°C for 5 min

PSMA-11 labelling

-10 µg peptide

-acetate buffer: 1 mL 1.5 M (pH 4.5)

- heated at 95°C for 5 min

^{68}Ga-DOTA-NOC purification

- HLB cartridge / washed with 10 mL of water

^{68}Ga-PSMA-11 purification

-Sep-Pak® Light C18 cartridge/- washed with 10 mL of water

^{68}Ga-DOTA-NOC formulation & sterile filtration

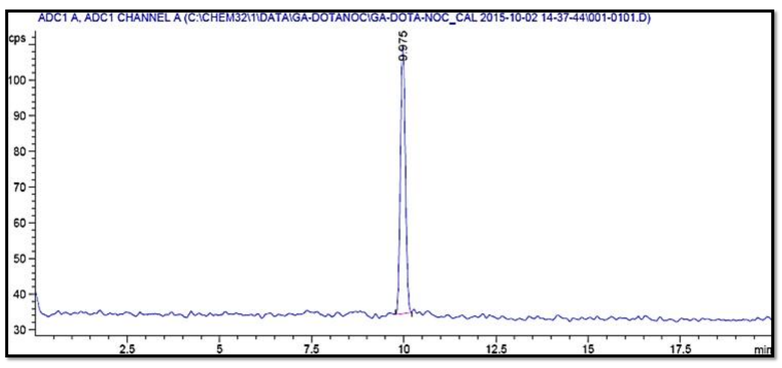
- Elution: 1 mL of EtOH/water 65:35 v/v to pre-loaded vial (8mL saline solution) through 0.22µm filter (Millex®-GV)

^{68}Ga-PSMA-11 formulation & sterile filtration

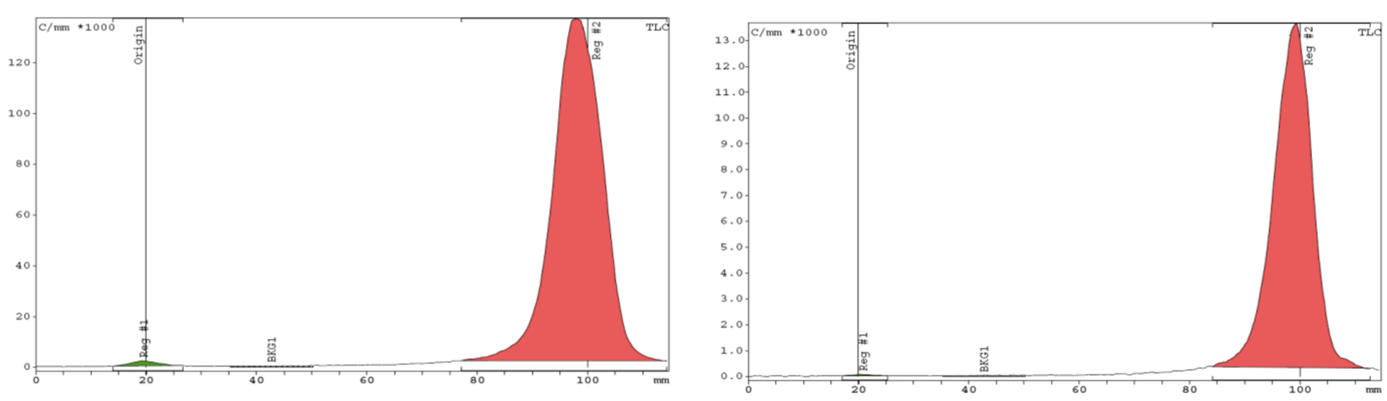
- Elution: 2 mL of EtOH/water 1:1 v/v mix + 2 mL PBS to pre-loaded vial (6 ml PBS) through 0.22µm filter (Millex®-GV)

Results

^{68}Ga-DOTA-NOC is produced in <20 min with 81.5±5.2 % radiochemical yield (RCY) (decay-corrected-d.c.) and ^{68}Ga-PSMA-11 is produced in 13 min with 97.4±2.5 % RCY (d.c.). Reported process times include generator elution and formulation. In both cases, final products show high radiochemical purity (TLC > 97 % and 99 % respectively).



Radio-HPLC analysis of ^{68}Ga-DOTA-NOC (Rt: 10 min)
HPLC methods are performed with Agilent Eclipse XDB-C18 (5 µm, 4.6 x 150 mm) (reverse phase column at flow rate of 2 mL/min. Eluent: A=Water/TFA 99.9:0.1 v/v ; B=ACN/TFA 99.9:0.1 v/v
Gradient: 0 min 25%B + 75%A; 4 min: 25%B + 75%A; 10 min. 32% B + 68% A; 14 min. 50%B + 50%A; 15 min. 25%B+ 75% A, 20 min. 25% B+ 75% A.



Radio-TLC analysis of ^{68}Ga-DOTA-NOC (left) and ^{68}Ga-PSMA-11 (right)
Radio-TLC were performed with Agilent iTLC-SG silica gel plate.
Eluent: Ammonium acetate 1 M and Methanol (50:50)

Discussion & Conclusion

Automated processes for the production of both ^{68}Ga-DOTA-NOC and ^{68}Ga-PSMA-11 have been successfully achieved using a commercial synthesizer and a ^{68}Ge/^{68}Ga generator. The labeling procedures are straightforward and efficient, thanks to the low elution volume and high purity of the generator eluate (no need for fractionation or post-elution purification).