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-Eilit, Fleurus, Belgium) have been developed in this work.

Materials & Methods

$^{68}$Ge/$^{68}$GaGenerator elution
- 1.1 ml – 0.1 M HCl
- No pre-purification required
- Eluate sent directly to the IBA Synthera® reaction vessel

$^{68}$Ga-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

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/TFAX99.9:0.1 v/v; B-ACN/TFAX99.9:0.1 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%+ 75%A, 20 min. 25%B+ 75%A.

$^{68}$Ga-PSMA-11 purification
- Sep-Pak® Light C18 cartridge:
  - Washed with 10 mL of water

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±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).

$^{68}$Ge/$^{68}$Ga-DOTA-NOC formulation & sterile filtration
- Elution: 1 mL of EtOH/water 65:35 v/v to pre-loaded vial (6 ml saline solution) through 0.22µm filter (Millex-GV)

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 labelling 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).