

## Radiopharmaceutical production of $^{68}\text{Ga}$ -PSMA at the National Cancer Institute. Bogotá-Colombia.

Tuesday, 29 October 2019 22:00 (15 minutes)

### Background

$^{68}\text{Ga}$ -prostate-specific membrane antigen (PSMA) radioligand diagnostic is a novel diagnostic option in patients with metastatic prostate cancer. The aim of this work was to standardize an efficient automated synthesis method for radiolabeling radiopharmaceutical-grade  $^{68}\text{Ga}$ -PSMA for PET/CT diagnosis of prostate cancer.

### Methods:

We employed PSMA-HBED-CC (PSMAHBED) peptide manufactured according to GMP requirements (purity >96%) obtained from ABX (Advanced Biochemical Compounds) and 1850 MBq ITG  $^{68}\text{Ge}/^{68}\text{Ga}$  generator consisting of organic-matrix column metal free. Sodium acetate, ascorbic acid, NaCl, HCl Ultrapur and EtOH was obtained from Merck

Automated synthesis module "Taddeo" from COMECER was installed in a shielded Hot cell and used for radiolabeling. The  $^{68}\text{Ga}$  solution was eluted from the generator with 7mL of 0.1M HCl at a flow rate of 2.5mL/min and transferred to a PS-H+ column and eluted with 5M NaCl (1.8mL). The total  $^{68}\text{Ga}$  activity (1400MBq) were transferred directly into the reaction vessel containing 5 $\mu\text{g}$  PSMA-HBED-CC peptide, dissolved in 1mL of Acetate buffer 1.0M with pH 4 and Ascorbic acid 10 $\mu\text{L}$ , heated to 92°C per 8 min. To process the radiolabeling product Strata-X-tubes pre-conditioned (Phenomenex) were used. The  $^{68}\text{Ga}$ -PSMA-HBED-CC was retained and unreacted  $^{68}\text{Ga}$  passed through into a waste vial. The Strata-X-tubes were then washed with 5mL of pure water and the  $^{68}\text{Ga}$ -PSMA HBED-CC was recovered with 1.2mL EtOH/Water (1:1) followed by 10 mL of 0.9% saline. Finally the product was sterile-filtered under aseptic conditions through 0.22 $\mu\text{m}$  membrane filter (Millex-GV, Millipore) and the activity was measured in a Capintec-CRC-15R dose calibrator.

The radiochemical purity and identity of the  $^{68}\text{Ga}$ - $^{68}\text{Ga}$ -PSMA solution was assessed by RP-HPLC equipped with a UV and  $\gamma$  detector. A Lichospher-100 column C-18 (25mm x 4.6mm, 5 $\mu\text{m}$ ), was used as stationary phase. The mobile phase was as follows: 0-0.5min: 95%B; 0.5-10min: a linear gradient 80% A, flow rate 2mL/min (6). Retention times were 1.5- 2.0 min for free  $^{68}\text{Ga}$  (III) and 4.9- 5.1 the thermodynamically more stable diastereomer (RR), 5.2- 5.4 the thermodynamically less stable.

An indicator strip was used for the pH analysis of the  $^{68}\text{Ga}$ -PSMA dose and the Bacterial endotoxin content was analyzed using an Endosafe R system (LAL test), the values limit were <175/IU/mL. The sterile filter integrity test of the  $^{68}\text{Ga}$ -PSMA solution was performed with a limit value >50psi

$^{68}\text{Ge}$ -contamination was detected and quantified using a gamma counter (at full open window and at a 1min measurement time) retaining the preparation for at least 48h to allow  $^{68}\text{Ga}$  to decay to a level allowing the detection of the impurities. The total radioactivity due to  $^{68}\text{Ge}$  must not be >0.001% referred to the original activity.

Radionuclidic identity and purity tests were performed by gamma-ray spectrometry and the principal gamma peaks analyzed, energies of 511Kev and 1077Kev were only allowed. The physical half-life was measured 3 times using a Capintec-CRC-15R Radioisotope Dose Calibrator. The half-life must be 62-74min.

Sterility test was performed by an external laboratory, according to the current US-pharmacopoeia.

### Results:

The synthesis of  $^{68}\text{Ga}$ -PSMA-HBED-CC parameters were optimized as described previously with 75%  $\pm$  5% decay corrected radiochemical yield. The production of  $^{68}\text{Ga}$ -PSMA-HBED-CC was within 28 min  $\pm$  1. Over the study period we made 52 synthesis of  $^{68}\text{Ga}$ -PSMA-HBED-CC. The radiochemical purity was >99.7% as two diastereomers, with pH range 5.5-7.0. The  $^{68}\text{Ge}$  impurities was found to be <0.0010% in the radiolabelled compounds. All samples passed the bacterial endotoxin test at values <10IU/mL and the sterility test. The residual solvent of the final product was ethanol in less than 10%. Up date we have injected 45 patients.

Conclusion: We have shown that it is possible to perform an automated synthesis to  $^{68}\text{Ga}$ -PSMA-HBED-CC using an Automated synthesis module "Taddeo" from COMECER ensuring a quality and high radiochemical yields and radiochemical purity > 99.7%.

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