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Development of ^{68}Ga Generator at ANSTO

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A ^{68}Ge/^{68}Ga generator combined with an automated ^{68}Ga eluate purification unit was developed to produce ^{68}Ga solution suitable for labelling peptide ligands for PET radiopharmaceutical applications. The sorbent of a Ti-Zr ceramic structure [1] was used as a generator column packing material. The SEM picture of micro- and meso-porosity of these materials is shown in Figure 1a. Its X-ray diffraction presents a tetragonal nano-crystalline structure.
The adsorption capacity for Ge^{4+} ions is approximately 120 mg Ge per gram sorbent in 0.1 M HCl solution. The distribution coefficient Kd > 10000 mL /g for carrier-free $^{68}Ge^{4+}$ ions and 2 mL/g for $^{68}Ga^{3+}$ were evaluated in 0.1 M HCl solution. A 1.0 g weight sorbent column was used for immobilizing the parent nuclide ^{68}Ge and ^{68}Ga was eluted from the column with 3- 4 mL 0.05 – 0.1 M HCl solution. The ^{68}Ge breakthrough in ^{68}Ga eluate was around 10^{-3} % for a generator of 18 mCi ^{68}Ge activity.

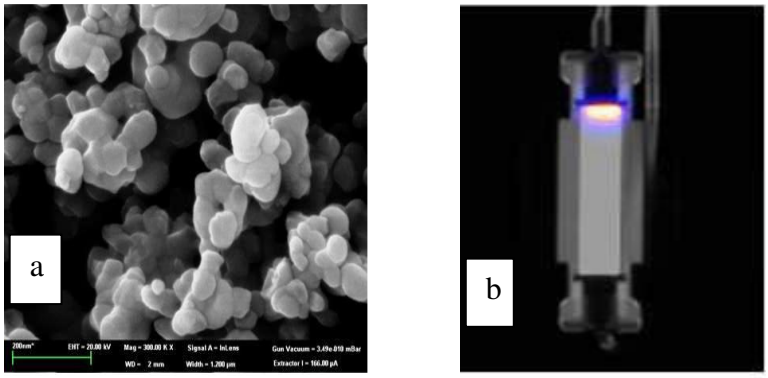

Figure 1. (a) SEM picture of Ti-Zr ceramic sorbent used for loading ^{68}Ge/^{68}Ga generator column; (b) PET imaging of the ^{68}Ge/^{68}Ga generator column after 300 ^{68}Ga elution cycles

The PET imaging picture of the ^{68}Ga generator column after 300 elution cycles (Figure 1b) showed no significant spreading and drift of ^{68}Ge zone along the column.
^{68}Ga eluate of around 5 mL volume in 0.1 M HCl solution was purified on a small cation exchanger column with an aqueous alcohol solution mixture of hydrochloric acid, ascorbic acids and halide salts. An alkali solution was used for elution of ^{68}Ga from the ion exchange resin column to obtain a purified ^{68}Ga solution which is conditioned with acidic solution to obtain a final ^{68}Ga product of pH=3-4 in 0.75 mL

0.5 M NaCl or 0.5 M sodium acetate solution. The metallic contamination <20 nano grams per mL were found in this product solution. The organic solvent free ^{68}Ga solution product of acidity suitable for coordination chemistry based labelling of the peptide ligands was successfully used for preparation of DOTATATE and DOTATOC PET radiopharmaceuticals.

The process of ^{68}Ga elution from the generator followed by ^{68}Ga eluate purification was performed using a low-cost automation bench-top system [2]. This system is designed (Fig. 2) based on the timing sequence of seven processing steps without feedback control. The variable flow rate of eluents used for elution/purification in this system also ensure the optimisation of operating times with respect to different adsorption/ desorption kinetics of ^{68}Ga ion species, which is controlled by the sorbent and ion exchange resin used in the generator and purification columns.

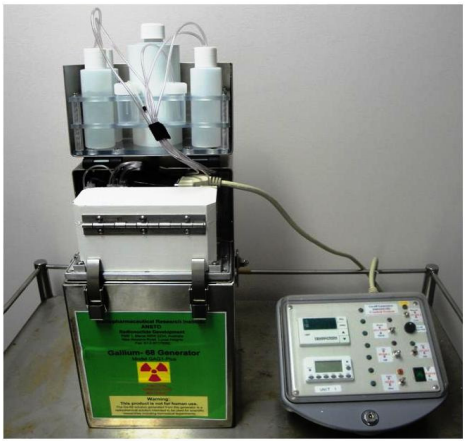

Figure 1: ^{68}Ga generator (housed in the lead container in the lower part of the system) and processing unit with the eluents for ^{68}Ga eluate purification (in the upper part) together with a control unit at the bottom right.

References

1. Van So Le, Sorbent material, Patent, PCT/AU2011/000245
2. Van So Le, ^{68}Gallium purification, Patent, PCT/AU2011/000244