Post-processing of $^{44}Ti/^{44}Sc$-radionuclide-generator for medical application

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Introduction: The $^{44}Ti/^{44}Sc$ generator provides cyclotron-independent access to positron-emitting ^{44}Sc for application in PET radiopharmaceuticals. The ^{44}Sc solution that can be obtained from generator is too diluted and too acidic for use in direct labeling procedures. The aim of this work was to design and to analyse the performance of a $^{44}Ti/^{44}Sc$ radionuclide generator for medical application.

Experimental: Post-elution processing studies were performed to reduce the volume and acidity of ^{44}Sc-eluate from $^{44}Ti/^{44}Sc$ generator and to reduce amount of ^{44}Ti in the final product for the syntheses of ^{44}Sc-labelled radiopharmaceuticals. It was developed, similar to the one developed for the $^{68}Ge/^{68}Ga$ radionuclide generator [1].
The $^{44}Ti/^{44}Sc$ generator was eluted with 20 ml mixture of 0.005 M $H_2C_2O_4$/0.07 M HCl. The retention of the ^{44}Sc eluate was checked on micro-chromatography columns, filled with 80 mg of cation-exchange resin AG W50x8 (200-400 mesh, H^+-form). The columns were dried by passing air through them to remove the rest of eluate, then washed by 3 ml H_2O and dried once again. Several solutions at various volumes and concentrations were used to elute ^{44}Sc from the columns.
Finally micro-chromatography column (~2 mm inner diameter, ~5 mm length) was prepared using two 3-way valves filled with 53 mg of cationit. The $^{44}Ti/^{44}Sc$ radionuclide generator was connected to the valves via tubing. The ^{44}Sc-eluate mixture was transferred on-line within 20 min through the column. Subsequently, the column was washed by 3 ml H_2O and dried by air. Then, 3 ml of 0.25 M ammonium acetate, acidified to pH = 4.0 by drop-wise addition of acetic acid were passed slowly through the column and the ^{44}Sc eluate was collected in a 10 ml glass vial.
The aliquots of consecutive fractions were collected and measured according to the activity of ^{44}Sc and ^{44}Ti using dose calibrator and γ-spectroscopy.

Results: To reduce the volume of the ^{44}Sc eluate, a 3-valves cartridge with 53 mg of cationic resin AG W50x8 was connected with the generator on-line. Recently, the eluate passes through the cartridge and ^{44}Sc is adsorbed on the cationic resin, from which it can be eluted by 3 ml of 0.25 M ammonium acetate, pH=4.0. This solution is ready for labelling with peptides and other biomolecules. Finally, the cartridge is reconditioned by washing with 1 ml of 4 M HCl and 1 ml of water. The scheme of the generator together with post-elution processing is presented on Figure 1.

Conclusions: On-line post-elution processing of $^{44}Ti/^{44}Sc$-radionoclede generator is performed on the small cationic cartridge. In the final point, around 160 MBq of ^{44}Sc is obtained daily in 3 ml 0.25 M ammonium acetate buffer (pH=4.0). This solution can be used for labeling of biomolecules.

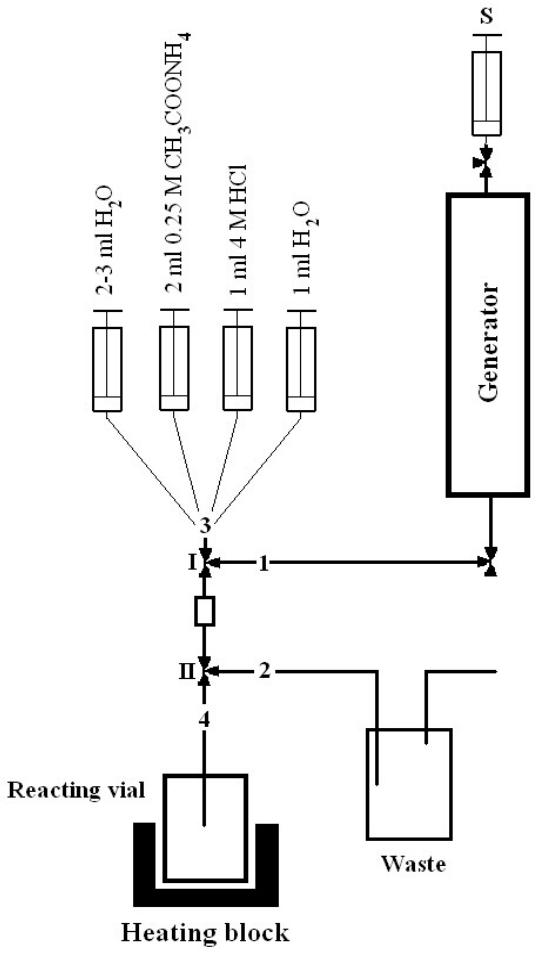

Figure 1. Scheme of the $^{44}Ti/^{44}Sc$ generator together with post-elution processing of ^{44}Sc-eluates and generator-associated syntheses of ^{44}Sc-labeled compounds.

References:
[1] K.P. Zhernosekov, D.V. Filosofov, R.P. Baum, P. Aschoff, H. Bihl, A.A. Razbash, M. Jahn, M. Jennewein, F. Roesch, Procesing of generator-produced ^{68}Ga for medical application, J. Nucl. Med. (2007), 48, 1741 – 1748.

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